A COMPARATIVE STUDY OF ORAL MIFEPRISTONE AND ENDOCERVICAL PGE_2 GEL AS PREINDUCTION CERVICAL RIPENING AGENT IN PARTURITION

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CERTIFICATE

This is to certify that the dissertation entitled "**A COMPARATIVE STUDY OF ORAL MIFEPRISTONE AND ENDOCERVICAL PGE_2 GEL AS PREINDUCTION CERVICAL RIPENING AGENT IN PARTURITION"** is the bonafide original work of **Dr. B. Arumugaselvi** under the guidance of **Prof. Dr. H.K. Fathima MD, DGO, HOD,** Department of Obstetrics and Gynecology, K.M.C.H. Chennai in partial fulfillment of the requirements for the degree of M.D branch II Obstetrics and Gynecology examination of the Tamilnadu Dr. M.G.R Medical University to be held in March 2010.

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LIST OF ABBREVIATION

ACOG	-	American College of obstetrics and gynecology
RCOG	-	Royal College of obstetrics and gynecology
PGE_1	-	Prostaglandin E_1
PGE_2	-	Prostaglandin E_2
$PGF_2\alpha$	-	Prostaglandin F_2 alpha
IUD	-	Intra uterine death
ARM	-	Artificial rupture of membrane
GI - SYMPTOMS	-	Gastrointestinal symptoms
PPH	-	Post partum haemorrhage.
MAS	-	Meconium aspiration syndrome
NICU	-	Neonatal intensive care unit
NN Mortality	-	Neonatal mortality
PR	-	Progesterone receptor

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INTRODUCTION

INTRODUCTION

Human parturition has been termed ‘labour’ in recognition of the hard work that the parturient as well as the uterine myometrium have to perform in order to deliver the fetus. Labour refers to the onset of effective uterine contractions leading to progressive effacement and dilatation of the cervix resulting in the expulsion of the fetus, placenta and the membranes.[1]

According to Turnbull (1976)- **“The spontaneous onset of labour is a robust and effective mechanism…. And should be given to operate on its own. We should only induce labour when we are sure that we can do better”**

The most important decision to be made when considering induction of labour is whether or not the induction is justified. How it is to be achieved, is a secondary decision. Whatever method is chosen to implement a justified decision to induce labour, uterine contractility and maternal and fetal wellbeing should be monitored closely.

In the present world, there is a spectrum of valid indications for induction of labour. The concept of elective induction for the convenience of the obstetrician and the patient, is not recommended by the ACOG at present,

but this practice is recommended or indicated when the benefits for the mother and fetus outweigh those of continuing the pregnancy and to achieve vaginal delivery, thus avoiding an unnecessary caesarean section[2].

The present day obstetrics, calls for induction for a myriad of obstetrical, medical and fetal indications, that include valid indications which include emergency situations like premature rupture of membranes with chorioamnionitis, severe preeclampsia etc., to several relative indications which may amount to or approximate an elective induction such as a residence at an appreciable distance from an obstetric facility or history of rapid labour in the previous pregnancy[3] .

Compromise to maternal longevity, accounts for the majority of indications for induction of labour, while the wide diversity of fetal indications are most often not compromising to their survival or morbidity. Favourability of the cervix is a need for labour induction. Research in this direction has helped in the development of various methods to 'ripen' the cervix prior to uterine contractions. The discovery of prostaglandins, and lately the antiprogesterones, have made labour induction at the disposal of the obstetrician, enabling the delivery of the patient as and when required, thus allowing a carefully planned active management, and in bringing down the

trauma of a prolonged or protracted and painful labour for the patient, to give her a healthy baby without compromising her health.

AIM OF THE STUDY

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1. ***To compare the efficacy and safety of oral mifepristone, and endocervical PGE2 gel for preinduction cervical ripening in term pregnancies and prolonged pregnancies.***

2. ***To evaluate the effect of these drugs on parturition and neonatal outcome.***

3. ***To critically evaluate the effect of these drugs on primigravida and multigravida.***

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Induction of labour:

Induction of labour is one of the most commonly performed interventions in modern obstetrics with upto 20% of pregnant women having labour induced in some countries.

Induction can be defined as an intervention intended to artificially initiate uterine contractions resulting in the progressive effacement and dilatation of the cervix which will result in the birth of the baby by vaginal route.

Induction rates have been influenced by several reports worldwide, which claimed that an active induction policy, led to substantial reduction in perinatal and maternal morbidity and mortality.

The incidence of induction of labour varies widely in different parts of the world. It is 10-15% in developing countries and 10-25% in the developed world. At Parkland Hospital, approximately 30% of labour were induced or augmented using oxytocin.

History of Induction of Labour:

History of labour induction, antedates back over the past three to four centuries, which has been accomplished by an innumerable number of mechanical and pharmacological methods. This exhaustive list is enumerated below.

I. Mechanical Methods:

1. ***Amniotomy or artificial rupture of memberanes or the ENGLISH METHOD*** was the first really effective method of induction of labour, practised by Thomas Denman in 1756. Scheel's method
2. ***Electricity for labour induction*** (Herder 1802, Schreiver 1843, Renford 1842, Henning 1856, Theobald 1973)
3. ***Stripping or sweeping of membranes by using the forefinger*** (Hamilton 1810)
4. ***Massage of the uterus*** (Uslamer and d'Outrepont 1820)
5. ***Massage of the breasts*** (Friedricgh 1939)
6. ***Sponge tents in the cervix*** (Brunninghousen 1820)
7. ***Instrumental dilatation of the cervix*** has been an age-old method.
8. ***Vaginal tampoons*** (Scholler 1842)
9. ***Cervical tampoons*** (Kehrer 1888)

10. ***Extraamniotic injection of fluid*** or the **COHEN'S METHOD** (1846) or Glycerin (Pelzer 1891) and Artes' Paste.
11. ***Introduction of a catheter*** or the **KRAUS' METHOD** (Moir 1855)
12. ***Hot vaginal douche*** (Kinisch 1856)
13. ***Hot carbolic douche*** (Scanzoni 1856)
14. ***Rubber bags in the cervix*** (Barnes 1861)
15. ***Matreurynter*** (Tarnier 1862), small rubber balloons made of pig's bladder.
16. ***Hygroscopic cervical dilators*** (Kramner 1995, Gilson 1996)
17. ***Laminaria tent*** (Wilson 1865)
18. ***Balloon catheter for cervical dilatation*** (Baners and Woodman 1863)
19. ***Paracentesis of amniotic fluid usually with injection of irritant solutions***
20. ***Extra amniotic saline infusion*** – **EASI** (Schreyer 1989)

II. Pharmacological Methods:

1. ***Oxytocin*** was the first polypeptide hormone synthesized, which was an important milestone in labour induction. Its discovery won a Nobel prize for Du Vigneaud in 1953 and the efforts of Turnbull and Anderson (1968) led to its acceptance in routine obstetric practice.

However, it was noted that this method of induction resulted in more postpartum hemorrhage than induction with prostaglandins (Howarts and Botha 2001). When compared to induction with prostaglandins, evidence suggests that oxytocin induction is associated with a lower chance of delivery within 24 hours; there was no difference in the rate of cesarean section. However, subgroup analysis reveals more information showing that:

- In primigravid women, there is a reduction in the number of women satisfied with the method of induction when oxytocin is used.

- In women with an unfavorable cervix, that oxytocin induction is associated with a higher rate of cesarean section

- In women with a favorable cervix, induction with oxytocin was associated with greater satisfaction.

2. The discovery of Prostaglandins in the 1930's from human semen and its elucidation in the biological role in the parturition process, has revolutionized the process of labour induction and has been the greatest armamentorium in the induction of labour for the present day obstetrician.

Prostaglandins are autocoids detected in almost all tissues and body fluids including lungs, heart, stomach, adrenals, liver, spleen, kidney, central

nervous system, uterus, vesical gland and seminal fluid. Named by Von Euler of Sweden in 1935, who extracted it from the seminal vesicle. Sune Bergstrom of Sweden received a Nobel Prize for its synthesis in 1932.

Most protocols recommend the use of intracervical prostaglandin in women with an unfavourable cervix and intact membranes; however, there are benefits in giving prostaglandin to all women undergoing induction regardless of cervical score. Meta-analysis by the Clinical Effectiveness Support Group at the Royal College of Obstetricians and Gynecologists showed improved rates of successful vaginal delivery, lower rates of cesarean section and higher levels of maternal satisfaction in women induced with prostaglandin compared to oxytocin. However, amniotomy and oxytocin infusion are effective in women with a favourable cervix and in areas where resources are limited, the cheapness of this method may outweigh the consideration of maternal satisfaction. Vaginal PGE_2 tablets appear to be as effective as gel formulations and their use may offer financial savings. In 1992 FDA approved PGE2 (0.5mg intracervically) for cervical ripening and labour induction.

Misoprostol is a synthetic analogue of prostaglandin E1 and is less expensive, more stable and easier to store than PGE_2. These factors have led to the suggestion that misoprostol will allow the use of prostaglandin for

induction in areas of the world that have previously been unable to afford this luxury (E1 Refaey and Jauniaux 1997). In the UK and the USA, the drug currently has a licence for the treatment of peptic ulceration but has no licence for the induction of labour[28]. Although the manufacturers have indicated that they do not intend to pursue licensing for this purpose, the American College of Obstetricians and Gynecologists has issued statements that misoprostol is a safe and effective drug for the induction of labour when appropriately used (ACOG 1999, 2000)[2]. In the UK the Royal College of Obstetricians has remained more cautious, agreeing that misoprostol is a cheap and effective agent for inducing labour but due to safety concerns, feel that further clinical trials are required prior to recommending it's use in general obstetric practice (RCOG 2001a).

3. Mifepristone or RU 486, an antiprogesterone is a receptor level antagonist, licensed in the U.K in July 1991. Mifepristone is a 19-nor-steroid with a great affinity for the progesterone receptor and thus blocks the action of progesterone at a cellular level. As a fall in the level of progesterone is considered one of the important events in the onset of spontaneous labour, it therefore seems likely that this drug may be useful in induction[4]. A number of studies have looked at the efficacy of mifepristone in cervical ripening. When compared to placebo, 200mg oral mifepristone increases the chances of spontaneous labour and reduces the

need for prostaglandins (Lelaidier et al 1993)[18]. There is a reduction in the induction delivery interval when induction is performed after mifepristone and a trend to a reduction in the rate of cesarean section (Wing et al 2000)[17].

These studies in recent literature over the last two decades, shows the efficacy of mifepristone not only in first and second trimester induced medical abortions, but also its use of late, as a safe, orally effective cervical ripening and labour inducing agent.

Other Therapeutic Agents:

Purified Porcine Ovarian Relaxin (1-4mg)

Relaxin has been used both vaginally and intracervically to induce labour but studies have failed to show any benefit compared to prostaglandin (Kelly 2002b)[1].

Hyaluronidase

Hyaluronidase given by cervical injection has been postulated to increase cervical softening by increasing tissue water content. The problems associated with its administration and the lack of evidence of any benefit associated with using it, is such that its use cannot be recommended.[1]

Estradiol

Estradiol in tylose gel is not commonly used as an induction agent but has been used previously in the belief that they may stimulate prostaglandin release. There is no evidence to confirm or refuse their efficacy and their use is therefore of historical interest only.

Indications for Induction of Labour

The indications for induction of labour are, where the benefits of delivering the fetus at a specified point of time, outweighs the benefits of allowing the pregnancy to continue.

There are two main types of induction, namely Indicated Induction and Elective induction.

A.Indicated Induction [3]

Commonly accepted indications

- Pregnancy induced hypertension
- Prelabour rupture of membranes
- Chorioamnionitis
- Severe intrauterine growth restriction
- Isoimmunization
- Maternal medical problems

    Diabetes mellitus

    Renal disease

    Lupus

- Fetal demise
- Prolonged pregnancy
- Oligohydramnios

B. Elective induction

Logistic factors such as distance from the hospital or a history of rapid labor and delivery, may be reasonable indications. But elective induction (without medical or obstetric indications) is generally not recommended.

Contra indications

1. When vaginal delivery is contraindicated-

   (a) Major degrees of cephalo pelvic disproportion

   (b) Previous VVF repair

   (c) Pelvic tumour

   (d) Carcinoma cervix

   (e) Previous uterine surgery disruption

   (f) Active gential herpes infection.
2. Malpresentations.
3. Placental abnormalities like Vasa praevia and Type III and IV placenta praevia.
4. Appreciable macrosomia
5. Severe hydrocephalus
6. Non reassuring fetal heart rate

Outcome of Induction

Factors influencing the outcome of induction

The process of prelabour cervical softening and dilatation is a part of a continuum, which culminates in spontaneous labour.

The success of any method of induction depends largely on (1) Parity and (2) The state of cervix at the beginning of induction. In most centers, the modified Bishop score (1964) is used to assess the favourability of the cervix both prior to and following induction.[5] The partogram aids in assessing the progess of labour.

Some definitions, useful for assessing the success or failure of induction are enlisted below.

Successful induction

Successful induction is defined as **("Vaginal delivery of an infant in good condition with minimum maternal discomfort and side effects, within a specified framework of time").**

Failed induction

Defined by Duff et al (1984), **(as the failure to enter the active phase of labour, after twelve hours of regular uterine contractions).** Failed induction, is diagnosed when, a patient who was induced, does not deliver

vaginally, in the absence of fetal distress, with acute events like abruption or cord prolapse and failure of progress due to cephalopelvic disproportion or malposition and or if the patient has not entered the active phase of labour despite adequate management for twelve hours (Arulkumaran et al 1985).

Methods of Induction

There are only three existing broad approaches in induction of labour practiced in the current obstetric practise. They are:

(A) Amniotomy or Artificial rupture of membranes

(B) Use of oxytocic agents

(C) Stripping of membranes or Sweeping of membranes.

(A) Amniotomy or Artificial rupture of membranes

Introduced by Thomas Denman more than 200 years ago, the procedure represents one of the most irrevocable interventions in pregnancy, and more than any other procedure calls for a firm commitment to delivery within a short time scale to avoid the risk of maternal and fetal infection.

Amniotomy alone often results in vaginal delivery in most women with good cervical score. However Patterson in 1971 found that 15% of primigravidas and 22% of multigravidas were not in established labour more than 24 hours after amniotomy. Therefore in current obstetric practice,

amniotomy is usually combined with oxytocin immediately or after a variable interval. After controlled artificial rupture of membranes without dislodging the presenting part amniotic fluid is allowed to drain, color of liquor and any cord prolapse is noted.

There are two types of rupture of membranes – ***Low rupture of membranes*** **(LARM)** done by using a kocher's artery forceps and high rupture of membranes or hind water amniotomy done by using a Drew-Smythe catheter. The low rupture of membranes is the basic procedure in induction of labour.

Prerequisites

- Vertex presentation
- Cervix must be well applied to the presenting part
- High Bishop score
- No cephalopelvic disproportion.

Mechanism of action

1. Releases endogenous prostaglandin and may result in labour.
2. Intrauterinespace decreases progressively following amniotomy so that the uterine muscles contract more efficiently.

Complications

Are mainly in the form of infection, chorioamnionitis, cord prolapse, premature separation of placenta, injury to the fetus and cervix constant drainage of liquor amni, fetal anaemia due to unrecognized vasa previa, risk for Rh iso-immunisation.

(B) Stripping of membranes or Sweeping of membranes

Sweeping or stripping of the membranes is an old method of inducing labour described by Hamilton in 1810. Sweeping of the membranes involve the digital separation of the membranes from the lower segment and has been widely used for many years in the belief that it reduces the need for formal induction of labour. The procedure of membrane sweeping causes an increase in the levels of prostaglandin F_2alpha (McColgin et al 1993). Several recent studies have addressed the validity of this belief and the risks associated with this procedure.

In a randomized study of 195 women beyond 40 weeks, two-thirds of women undergoing membrane sweeping laboured spontaneously within 72 hours compared to one-third of women in the control group (Allot and Palmer 1993). A recent meta-analysis concluded that sweeping membranes prior to term (38-40 weeks) does reduce the frequency of prolonged pregnancy and reduce the need for formal induction of labour from 36 per cent to 21 per cent

(Boulvain et al 2001). The same review found no evidence of serious maternal or neonatal morbidity, such as infection associated with the procedure.

Technically, membrane sweeping is not possible in all women (Cammu and Haitsma 1998), usually requiring a cervical score greater than 4. Women undergoing membrane sweeping, more frequently describe discomfort during the vaginal examination, vaginal bleeding and contractions not associated with the onset of labour than women not undergoing sweeping (Boulvain et al 1999). This discomfort will not be tolerated by all women and counselling prior to membrane sweeping is needed.

Although it is presumed to be a formal method of induction, it is still employed by some obstetricians at term, especially when the indications for induction are not strong enough. The forewater is stripped by a gloved index finger passed through the cervical canal. Uterine contractions are frequently established following the procedure resulting from the release of endogenous prostaglandins, and labour is brought about within 3 days.

3. Oxytocin

Commonly used method of induction.

CERVICAL RIPENING

Cervical ripening is a process by which the cervix becomes soft, compliant and partially dilated. It is due to a combination of biochemical, endocrine, mechanical and possibly inflammatory events.

Cervix is composed of collagen, smooth muscle and connective tissue 'ground substance' containing glycosaminoglycans. Cervix is predominantly composed of types I (66%) and type III (33%). The firmness of the cervix in the non pregnant state is mainly due to the properties of these collagen fibrils which are bound together in the form of bundles. These bundles in turn are embeded in ground substance consisting of proteoglycans.[7]

In the cervix the main glycosaminoglycan are dermatan sulphate and chondroitin sulphate both of which are highly negatively charged and hydrophobic. Hence they repel water and are responsible for the firmness of the cervix. Towards term the glycosaminoglycan concentration of the cervix alters and the dermatan and chondroitin sulphates are replaced by hyaluronic acid. Hyaluronic acid is hydrophilic and imbibes water. Accumulation of water within the substance of the cervix destabilizes the collagen fibrils contributing to cervical ripening. The water content of human cervix increases from 80% in non pregnant state to 86% in late pregnancy.[1]

Collagenase is an enzyme that breaks down collagen types I, II and III and is produced by fibroblasts and leucocytes. Leucocyte elastase is another enzyme that that can break down elastin, collagen and proteoglycans. It is produced by macrophages, neutrophils and eosinoplils. The levels of both these enzymes are found to increase with advancing gestation and are associated with progressive decline in the concentration of cervical collagen.

Cervical remodelling takes place with advancing gestation. The mature collagen, which has many crosslinks that are responsible for its tensile strength, is replaced by an immature collagen, which has few such crosslinks. Functionally the newly formed immature collagen is much weaker and is easily broken down during labour.

Cervical Ripening Methods[3]

Mechanical Methods:

- Foley Catheter
- Laminaria tents
- Hygroscopic dilators
- Acupuncture
- Membrane stripping

Pharmacologic Methods

- Mifepristone (RU 486)
- Dinoprostone (PGE_2)
- Misoprostol (PGE_1)
- Nitricoxide
- Relaxin

Methods to assess cervical ripening

- Bishop score
- Lange score

Bishop Score

Parameters	0	1	2	3
Dilatation of cervix (cm)	0	1-2	3-4	5-6
Effacement of cervix (%)	0-30	40-50	60-70	80
Consistency of cervix	Firm	Medium	Soft	-
Position of Cervix	Posterior	Mid	Anterior	-
Station	-3	-2	-1,0	+1,+2

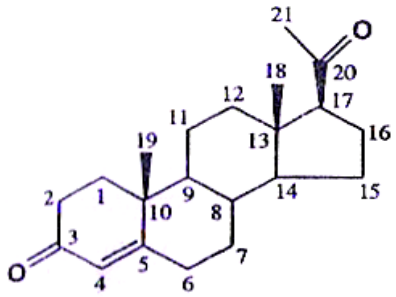
MIFEPRISTONE (RU 486)

Introduction:

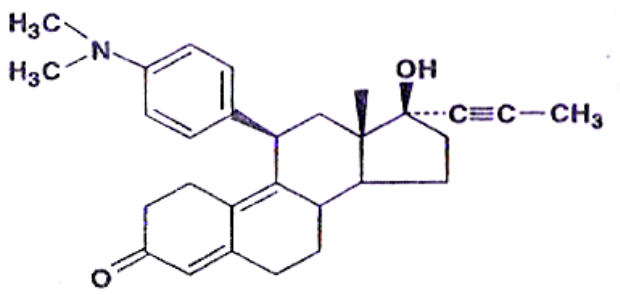
Mifepristone, a synthetic steroid was discovered in 1980 by Dr. Etienne – Emile Beaulieu of France. Mifepristone is an antiprogestin. There are two types of antiprogestin

- Type I -RU486, ZK 112993
- Type II – ZK 98299.

Structure:

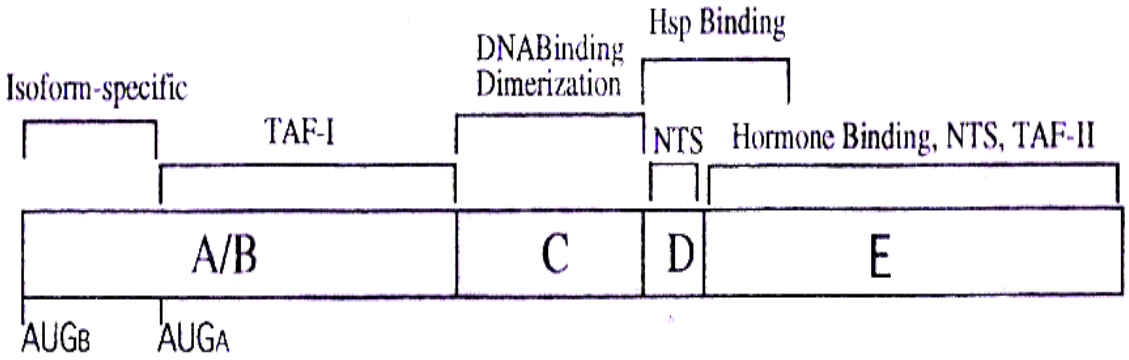


Progesterone



Mifepristone

Mifepristone is a 19 nor steroid, chemically referred to as 11 beta-(4-dimethyl amino phenyl)-4, 9-dien-3-one. It is an antiprogestrone. It has a molecular formula of $C19H35NO2^{6}$. Its molecular weight is about 429.6. The dimethyl amino phenyl side chain at position 11, which is a hydrophilic



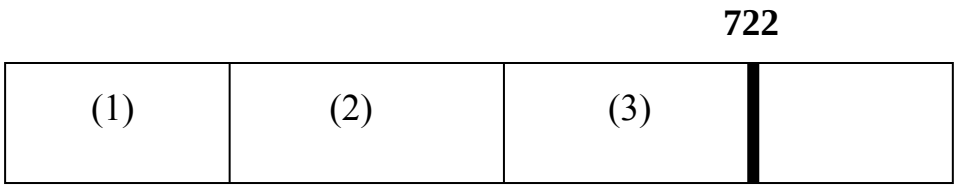
moiety, appears to be essential for the antiprogestronic activity. It also has antiglucocorticoid and antiandrogen activity.

The structure of the gene encoding both isoforms (PR_A and PR_B) of the progesterone receptor includes the location of the n-terminal initiation codon for each isoform (AUG_B and AUG_A)[8]. The basic structure of this gene is shared by all members of the steroid, thyroid, vitamin D, retinoic acid and orphan receptor superfamily, with five functional domains: an n-terminal transactivation domain (A/B), a DNA-binding domain (C), a hinge region (D) and a hormone-binding domain (E). Regions important for heat shock protein binding (HSP), nuclear translocation (NTS) and transcriptional activation (TAF-I, -II) are also indicated.[2]

Mifepristone acts as a competitive receptor antagonist at the progesterone receptor in the presence of progesterone and acts as partial agonist in the absence of progesterone. Mifepristone at doses greater or equal to 1mg/kg antagonize the endometrial and myometrial effects of progesterone. Antiglucocorticoid effect of mifepristone is manifested at doses greater or equal to 5.5mg/kg and antiandrogenic effect in animals is seen with prolonged administration of very high doses of 10-100mg/kg[24]

III. Receptor binding

Progesterone receptor schematic diagram.



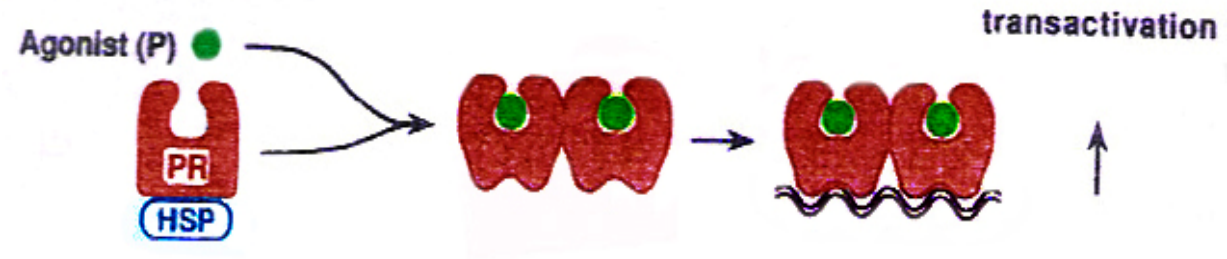
1. Transactivation domain
2. DNA binding domain
3. Hormone binding domain

The anti progestin action of mifepristone is mediated by the PR, a ligand activated transcription factor with domains for DNA binding, hormone binding and transactivation. The amino acid glycine at position 722, which is in the hormone-binding domain of the human PR, appears to be critical for mifepristone binding and action. Substitution of glycine with cysteine in the human PR generates a receptor that no longer binds mifepristone.

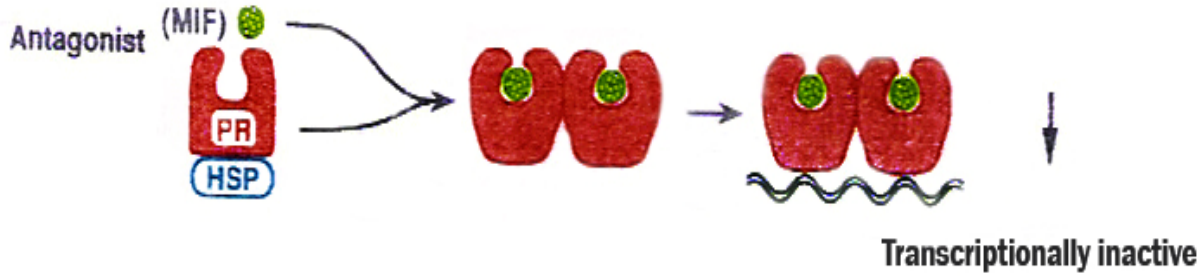
Mechanism of action

Progesterone and mifepristone produce a conformational change in the form of the PR that permits it to bind to DNA.

Agonist (Progesterone)



Antagonist (mifepristone)



PR – Progesterone receptor

HSP – Heat shock protein

In the absence of ligand the progesterone receptor is associated with heat shock proteins. Binding of progesterone or mifepristone induces conformational changes resulting in dissociation of HSP and dimerization of PR. The PR complex binds to specific progesterone response elements in the promoter regions of progesterone responsive genes. Progesterone – PR

complex is transcriptionally active resulting in agonistic effects whereas mifepristone – PR complex is not transcriptionally active resulting in antagonistic effects[39].

Under certain circumstances as in the absence of progesterone, mifepristone display progesterone agonistic activity It is related to the existence of two isoforms of PR, PR-A and PR-B. PR-B behaves as a partial agonist in the presence of mifepristone. When PR-A and PR-B are present together the antagonistic effects of PR-A can override the agonistic effects of PR-B. So agonistic or antagonistic action depends on relative expression of PR-A and PR-B in target tissues.

Pharmaco Kinetics

Mifepristone is administered orally and is readily absorbed. Metabolism in splanchnic circulation reduces its bioavailability to 40%. Metabolic clearance rate is 0.55l/kg / day. It doesnot bind to cortisol binding globulin or sex steroid binding globulin[31].

Serum mifepristone levels reached a maximum in one hour after oral administration of single dose ranging from 50 to 800mg. After single dose of 100mg or less the disappearance of mifepristone follows first order kinetics with a half life of 20-25 hours. After higher doses 200-800mg there is an

initial redistribution phase of 6-10 hours followed by a plateau in serum levels for 24 hours or more.

The major excretory pathway is fecal with less then 10% being recovered in urine. Metabolism involves two step demethylation and hydroxylation. Mifepristone metabolite cross the placental barrier during the second trimester, the efficacy of placental transfer decreases with advancing pregnancy.[23]

Clinical pharmacology:

Pregnant uterus

Mifepristone acts on receptors in decidua resulting in progesterone withdrawal to endometrium, disruption of placental function and uterine bleeding. Mifepristione stimulate release of $PGEF_2\alpha$.[33,46,47] The increase in prostaglandin is due to marked reduction in the activity and tissue concentration of prostaglandin dehydrogenase, the key enzyme involved in the control of prostaglandin catabolism by mifepristone[21].

Mifepristone increases the sensitivity of the myometrium to prosta glandin due to increase in number of gap junctions so that synchronization of uterine muscle contractility occurs. This causes enhanced electrical activity resulting in opening of voltage dependent calcium channels, which causes calcium influx and thereby muscle contraction.[53]

Mifepristone causes cervical ripening in women undergoing termination of pregnancy. Mifepristone causes cervical ripening directly or through the blockage of progesterone receptors[49.] Mifepristone stimulates the release of nitric oxide and the expression of inducible nitric oxide synthase in cervical cells of women. This is one of the mechanism by which mifepristone initiates cervical ripening[52].

Other Uses

1. Termination of early pregnancy

Medication abortion became an option for early abortion in India when in April 2002, the Drugs Controller General approved the use of mifepristone to terminate early pregnancies.

In December 2006, the Drugs Controller General of India granted the permission to manufacture misoprostol and approved its use for gynecological conditions like cervical ripening, prevention of post partum hemorrhage and first trimester abortion with mifepristone[50]. While in India, a combination of mifepristone and misoprostol is recommended for termination of early pregnancy up to 49 days/seven weeks from the last menstrual period (LMP); WHO recommends their use up to 63 days or nine weeks from LMP (WHO, 2003).[13]

Mechanism of action

Mifepristone is an anti-progestin, which stops the pregnancy from growing, detaches it from the lining of the uterus and softens the cervix.[51,52]

Recommended Drug Protocol		
Day 1	200mg mifepristone orally.	Anti D if Rh-ve
Day 3	400 mcg misoprostol orally/vaginally.	Analgesics
Day 15	confirm completion of abortion by USG	Contraceptive

2. Contraceptive

Mifepristone, a novel estrogen free contraceptive when administered in low doses daily (2 to 10mg), it inhibits ovulation, menstruation and significantly suppresses effects on the endometrium.[30] However, due to continuation of variable degree of follicular development, unopposed estrogen can cause hyperplastic or malignant changes in the endometrium. But in 2003, Baird ST et al, in their study reported that mifepristone<10mg per day neither caused endometrial hyperplasia nor the significant effect on the HPA-axis. Mifepristone also maintained bone density, lipids & sense of well being. Mifepristone as a postcoital contraceptive inhibits ovulation, blocks implantation by causing a delay in maturation of endometrium and causes regression of the corpus luteum in the majority of women when given in the middle or late luteal phase.[32,43,48] Two randomized trial have compared 600 mg of mifepristone with the Yuzpe regimen. In these trials single dose

of 600mg of mifepristone given within 72 hours of unprotected intercourse was 100 percent effective as an emergency contraceptive.[34]

3. Uterine myoma

For safe and effective non-surgical treatment of symptomatic fibroids, high-dose progestin therapy and GnRh agonists have been shown to decrease overall uterine volume by 50 percent at the end of 3 months therapy. So far no therapy has been used on a long term basis, therefore, the effect of medical therapy is temporary. On a long term basis, mifepristone blocks progesterone dependent growth factors, reduces blood supply due to vascular changes and decreases inhibition of progesterone estrogen receptor gene transcription by the progesterone receptor - A isoform, these are some of the mechanisms causing the antiproliferative activity of mifepristone. Mifepristone can be used in uterine fibroids as an alternative to GnRh anlogues in the preoperative application and if the safety of long term low dose mifepristone is established, perimenopausal women with large, symptomatic fibroid could avoid hysterectomies by using mifepristone till menopause.[41]

4. Endometriosis

Mifepristone through antioxidant property does not allow endometriosis to proliferate. It also preserves follicular phase levels of estradiol 5mg dose does not stabilize the endometrium and hence needs a

dose of 50mg daily. However, the use of mifepristone for the treatment of endometriosis requires additional studies.[42]

5. Ovarian Cancer

Mifepristone inhibits ovarian cancer cells growth by inducing G1 cell cycle arrest and blocking the G1-S phase transition without causing cell death. This growth arrest is observed by a decline in cyclin – dependent kinase 2 (cdk2) protein level and activity.[44] In 2003, Xu M et al reported that ovarian cancer cells expressed glucocorticoid receptors. Mifepristone may drive its anticancer action by binding to glucocorticoid receptors with an affinity similar to that for progesterone receptors and as an antioxidant to drive G1 arrest through a p53 independent p21. In 2000, Rocereto TF et al in their small trial conducted with 44 patients suffering from recurrent epithelial ovarian cancer whose tumors had become resistant to standard chemotherapy, mifepristone administration showed desirable effects against some of the tumors. Thus, mifepristone is a single agent potent blocker of ovarian cancer growth, however, the feasibility of using mifepristone to enhance the efficacy of conventional chemotherapy for ovarian cancer requires further investigations.

6. Premenstrual Syndrome

The sex steroid dependency of this disorder has been well established by the absence of PMS in castrated women and women treated with GnRH agonist analogues. Because the main symptom complex occurs in the luteal phase when serum progesterone is at the highest level, it was proposed that an antiprogestin, such as RU 486, may be useful in treatment of PMS.[40] Dosing schedules such as low dose daily administration to induce a acyclic pattern may yet prove to be efficacious in the treatment of PMS.

7. Ectopic Pregnancy

The role of antiprogestin in the medical therapy of ectopic pregnancy remains to be clearly defined. Certainly, the timing, dosing, and efficacy of RU 486 treatment in this scenario awaits future studies.

8. Abnormal Uterine Bleeding

It has been suggested by some that antiprogestins may be useful in treatment of dysfunctional uterine bleeding. No clinical experience in this venue has been published. If adenomyosis is the etiology of menorrhagia, it may be expected that treatment with an antiprogestin may be useful.

9. Breast Cancer

It has been observed that estrogen and progesterone in low doses stimulates breast cancer growth but in high doses both inhibit breast cancer growth. Tamoxifen, the antiestrogen, remains the first line therapy for

advanced estrogen-receptor-positive tumor because of its efficacy, safety and convenience. Antiestrogen (Tamoxifen) and antiprogestin produce tumor regression but either agent alone only produces tumor stasis. Tamoxifen down regulates the estrogen receptor but it favors agonists activities and therefore up regulates the progesterone receptor. Mifepristone down regulates both estrogen and the progesterone receptors. The finding suggests that tamoxifen can not inhibit the progestin-mediated growth-stimulatory effects. Thus, addition of mifepristone to tamoxifen effectively reestablishes tamoxifen growth inhibition. It has been observed that eventually all advanced breast cancer become hormone independent and increasingly resistant to any subsequent therapy as a result there is limitation in potential utility of antiprogestin and other endocrine therapies for the treatment of advanced disease.

10. Cushing's Syndrome

Chronic exposure to excessive corticosteroids in Cushing's Syndrome leads to the development of multiple metabolic abnormalities such as glucose intolerance, dyslipidemia, hypertension, osteoporosis and weight gain. In 2001, Dwight FM et al reported that extremely ill patient with Cushing's syndrome, treated initially unsuccessfully by a combination of conventional surgical, medical and radiotherapeutic approaches responded extremely well up to 25mg/kg/day, long term mifepristone, glucocorticoid receptor

antagonist therapy. Treatment efficacy was confirmed by the normalization of all biochemical glucocorticoid-sensitive measurements, significant reversal of the patient's heart failure, the resolution of the psychotic depression and usual return of his HPA axis to normal.[25]

11. Meningioma

Most meningiomas have no estrogen receptors but have substantial concentrations of progesterone receptors. In patients with unresectable meningiomas, objective response and subjective improvement has been noted.[29]

Contraindication

Mifepristone is contraindicated in the presence of an intrauterine device (IUD), ectopic pregnancy, adrenal failure, hemorrhagic disorders, inherited porphyria and anticoagulant or long term corticosteroid therapy.

Side Effects

Side effects of short term use include abdominal pain, cramping, nausea, vomiting and headache which are dose and treatment duration dependant. Long term administration of mifepristone is associated with adrenal insufficiency, low serum potassium levels, a slight increase in serum creatinine levels, moderate increase in hepatic enzymes and significant increase in thyrotrophins levels.

Conclusion

The combination of mifepristone plus a prostaglandin has been approved for ending pregnancies of up to 49days. The use of mifepristone plus an oral prostaglandin, presumably with fewer side effects,has improved the acceptability of this method for early first-trimester abortion over standard surgical procedure.Mifepristone has also been approved in France for the induction of labour in the event of fetal death Adequate clinical studies have demonstrated the safety and effectiveness of this drug and these studies support applications to regulatory authorities in other countries[9].Cochrane review has justified further trials comparing mifepristone with the routine cervical ripening agents currently used[53].

PROSTAGLANDINS

Structure

Prostaglandins are biological derivatives of 20 carbon polyunsaturated fatty acids that are released from cell membrane phospholipids. The prostaglandins PGE_2 and PGF_2 alpha are widely used in obstetric practice.

There are no preformed stores of prostaglandin. They are synthesized locally, in response to appropriate stimulus, at the rates governed by release of arachidonic acid from cell membrane by the action of lysosomal enzyme phospholipase A2, which is said to be the rate limiting step in prostaglandin biosynthesis.

Free arachidonic acid enters the cyclo-oxygenase pathway and converted to prostaglandin, by the enzyme prostaglandin synthase. In pregnant uterus of human being, free arachidonic acid is converted to prostaglandins in chorion leave and decidua vera, by prostaglandin synthetase specific activity, which is greatest in the amnion.

In the amnion and chorion, PGE_2 is formed. In decidua vera, both PGE_2 and F_2 alpha are formed. The fetal membranes and decidua vera are proved to be the site of synthesis of both arachidonic acid and prostaglandins in amniotic fluid. The half-life of primary prostaglandins is about five minutes while that of the major metabolite is 8 minutes. The lung is the

major site of metabolism of prostaglandins, other sites being the liver and kidney.

Pharmacological actions

Prostaglandins act on almost every other tissue in the body. Some of the best known actions are (a) stimulation of smooth muscle leading to either relaxation depending upon the receptors involved (b) changes in the cervical tissue (c) inhibition of gastric acid secretion and cytoprotection (d) inhibition and induction of platelet aggregation (e) increase in vascular permeability (f) thermoregulation (g) modification of steroidogenesis in the adrenals and gonads (h) inhibition of hormone induced lipolysis (i) release of neurotransmitters in the peripheral nervous system and the potentiation of action of biogenic amines.

However, the most potent action of prostaglandins is their ability to stimulate smooth muscles of the uterus, gut and vasculature. Unlike oxytocin, which is relatively ineffective in early pregnancy prostaglandins, are potent stimulators of uterine myometrium in all stages of pregnancy.

Uses of prostagandins in obstetrics include induction of abortion, termination of molar pregnancy, induction of labour, cervical ripening prior to induction of labour and abortion, acceleration of labour, management of atonic postpartum haemorrhage.

Muscle physiology consists of three important concepts: phasic contraction, tonic tension and relaxation. Phasic contraction is intermittent and may last for a short or a long period of time, whereas tonic tension is fairly constant lasting for prolonged periods. At the myometrial cellular level, prostaglandins have been found to induce both phasic contractions as well as tonic tension with superimposed phasic contractions (Chamley and Parkington 1984). In practical terms, they increase both the resting tone of the uterine myometrium as well as the amplitude and duration of myometrial contractions.

On a molecular level, phasic contractions are due to the influx of sodium ions into the myometrial cell, whereas tonic tension is due the increased availability of intracellular calcium. Both these processes are affected by prostaglandins (Reiner and Marshall 1976).

Prostaglandins also induce the formation of gap junctions between the myometrial cells, which help in the development of coordinated myometrial action, giving the advantages of a functional syncytium.

There is also a differential response according to the type of prostaglandins. PGE_2 metabolites peak prior to the onset of established labour, whereas PGF_2alpha metabolites peak during labour and correlate

directly with the duration of labour. PGE_2 has a predominant effect on the cervix, whereas PGF_2alpha on the myometrium.

Contraindications

(a) Hypersensitivity to the compounds

(b) Bronchial asthma

Advantages

(a) It has got powerful oxytocic effects, irrespective of the period of pregnancy. (b) As such it can be used independently especially in induction of abortion with success. (c) It is useful drug not only in induction but also for acceleration of labour. (d) it has no antidiuretic effect.

Disadvantages

(a) It is costly (b) Unpleasant side-effects caused by its stimulatory effects on the smooth muscles, which however subside easily due to its rapid metabolism (c) When used as an abortifacient, extensive cervical laceration may occur (d) The hyperactivity of the uterus if occurs during induction may continue for a variable period.

Side effects

(a) Nausea, vomiting and diarrhea are common. (b) Cramping pain of uterine origin related to the degree of uterine activity. (c) Unduly forceful uterine contractions. (d) Anaphylaxis.

Oxytocin

The word 'oxytocin' means "Quick birth". The structure of oxytocin was determined by Du vigneaud in 1950.

Oxytocin, an octapeptide which is secreted in a pulsatile manner is a neurohormone originating in the hypothalamus and secreted by the posterior lobe of pituitary gland. The half life is 10-12 minutes. The metabolic clearance rate is similar for men, pregnant women and non pregnant women. 20-27 m1/kg/minute. Recent study shows that 40 minutes are required for any particular dose of oxytocin to reach a steady state plasma concentration.[3]

The sensitivity of uterus to oxytocin increases as pregnancy progresses due to increase in oxytocin receptors in the myometrium and decidua. Oxytocin has direct stimulatory effects on the myometrium and also stimulates decidual prostaglandin production. The direct effect of oxytocin on myometrium is mediated by polyphosphoinositide hydrolysis with production of inositol phosphates that act as a second messenger and lead to the

mobilization of interacellular calcium ion. The principles of current clinical usage of intravenous oxytocin, are based on the classic studies of Turnbull and Anderson (1968).

Oxytocin is known to be a very potent uterotonic, causing uterine contractions in a sensitized uterus. The infusion of oxytocin is relatively ineffective in inducing labour in human pregnancies, except for dose near term. Oxytocin is effective, only in those patients in whom preparation of the uterus for active labour is already completed. The plasma concentration of oxytocin in pregnant women is 2-10mcg/ml.

Advantages

It is cost effective, relatively safe, the dosage can be adjusted and titrated according to the needs in a particular case, when combined with amniotomy induction delivery interval is very short, labour gets established earlier.

Disadvantages

Patient has to be confined to bed, in large doses it produces water intoxication, there are chances of hyperbilirubinemia, when given in higher doses, rarely it can cause rupture of uterus in multigravida and coronary insufficiency, and the incidence of PPH in induced labour is greater. Hyperstimulation, late deceleration of FHR can occur.[5]

Table.2.2: RCOG guidelines for induction of labour (2001)[1]

Time after starting (min)	Oxytocin dose (mu/min)	Volume infused (ml/hour)	
		Dilution 30 IU Oxytocin in 500 ml normal saline	Dilution 10 IU Oxytocin in 500 ml normal saline
0	1	1	3
30	2	2	6
60	4	4	12
90	8	8	24
120	12	12	36
150	16	16	48
180	20	20	60
210	24	24	72
240	28	28	84
270	32	32	96

MATERIALS AND METHODS

MATERIALS AND METHODS

Selection of cases

This comparative study done to compare the efficacy of oral mifepristone and endocervical PGE_2 gel as preinduction cervical ripening agents in term gestation and prolonged pregnancies was done in uncomplicated antenatal women who had clear indication for induction of labour, admitted in antenatal ward and labour ward at Government Kilpauk Medical Hospital, Chennai. 100 antenatal women were selected for study 50 women received oral mifepristone 200mg and 50 women received endocervical PGE_2 gel 0.5mg.

This comparative study was done after getting clearance from ethical committee of Government Kilpauk medical college, Chennai.

Inclusion Criteria

1. Singleton pregnancy in cephalic presentation.
2. Post dated uncomplicated pregnancy.
3. Term uncomplicated pregnancies with unfavourable cervix. (Bishop - score < 4)
4. Intra uterine fetal death.

5. Congenitally anomalous babies.
6. Term or post term pregnancies with no contraindications for vaginal delivery.
7. No contraindications for prostaglandins or mifepristone.
8. Primigravida less than 35 years and uncomplicated multigravida up to three pregnancies.
9. Intact membranes during the time of induction.

Exclusion Criteria

1. Premature rupture of membranes.
2. Malpresentations.
3. Cephalopelvic disproportion.
4. Bad obstetric history or history of previous abortions.
5. Previous history of caesarean section or any uterine surgery.
6. Associated medical complications.
7. Multiple pregnancy.
8. Elderly primigravida (age > 35 years).
9. Oligohydramnios.
10. Rh Negative mother.
11. Placental complications like abruption or placenta praevia.
12. Abnormal fetal heart rate patterns.
13. IUGR

14. Parity > 3
15. Active herpes infection.
16. Contra indication for prostaglandins.
17. Chorioamnionitis
18. Any febrile morbidity.

On admission, a detailed history, and complete general and obstetric examination was carried out. Vaginal examination was done under strict aseptic precautions and the cervical status, fetal station were assessed. Gestational age calculated by Naegle's rule and a routine obstetric scan for fetal maturity and well-being was done. Once the inclusion criteria were fulfilled and cephalopelvicdisproportion was ruled out, the patient was prepared and transferred to the labour ward. Indication for induction was noted after reaffirming that there was no contraindication for induction.

Informed Consent

A detailed written informed consent was obtained from the participant and her relatives. The following were addressed in the consent form. Indication for induction of labour, drug to be administered with its dosage and mode of administration, side effect of the drug, risks associated with the administration of these drugs and if complications arise, alternative mode of termination were all discussed.

Treatment Schedule

Group – I

50 pregnant women were given tablet mifepristone 200mg orally on day1. They were observed for maternal vitals, uterine activity bleeding or draining pv and fetal heart rate. After the wait period of 24 hours or when the Bishop score was ≥ 6, when the cervical dilatation was > 2cm, or when the membranes ruptured or when the patient was well in labour whichever is earlier labour was accelerated with oxytocin drip.

Group – II

50 pregnant women pregnant were instilled endocervical PGE_2 gel 0.5mg on day 1. They were observed for maternal vitals,uterine activity,bleeding or draining pv and fetal heart rate. After the wait period of 6 hours or when the Bishop score was ≥ 6, when the cervical dilatation was >2cm, or when the membranes ruptured or when the patient was well in labour whichever is earlier labour was accelerated with oxytocin drip.

Monitoring of the patients

Maternal vitals, uterine activity and fetal heart rate were monitored clinically. Partogram was maintained for all patients and used to record all the clinical events during the course of labour. A watch for the rupture of

membranes was done. If membranes not ruptured ARM was done at 3cm cervical dilatation. Pervaginal examination was done if there was rupture of membranes or once in 2 hours in active phase of labour. The pulse rate, blood pressure, temperature and urine output were recorded . Delivery particulars duration of each stage of labour blood loss at third stage of labour and baby particulars were recorded.Mother and baby were observed for postnatal complications if any.

Data were analysed and all the values were expressed as mean ± standard deviation or as percentages. Statistical comparison were performed by students paired and unpaired t-test and chi-square test. Statistically significant difference ($P<0.05$).

The efficacy was assessed by the following criteria:

1. Favourability of Bishop score at 24 hrs.
2. The need of oxytocin for augmentation.
3. Duration of I, II and III stage of labour and blood loss.
4. Drug administration to delivery interval.
5. The mode of delivery.
6. Cesarean section rate.
7. The 5 minute Apgar score, neonatal complications and incidence of neonatal mortality.
8. Maternal complications.

Success of induction was assessed by the following criteria:

1. Patients who delivered vaginally within 48 hours of the start of induction.
2. Bishop score of ≥ 6 at the end of 24 hours

Failure of induction was assessed by the following criteria:

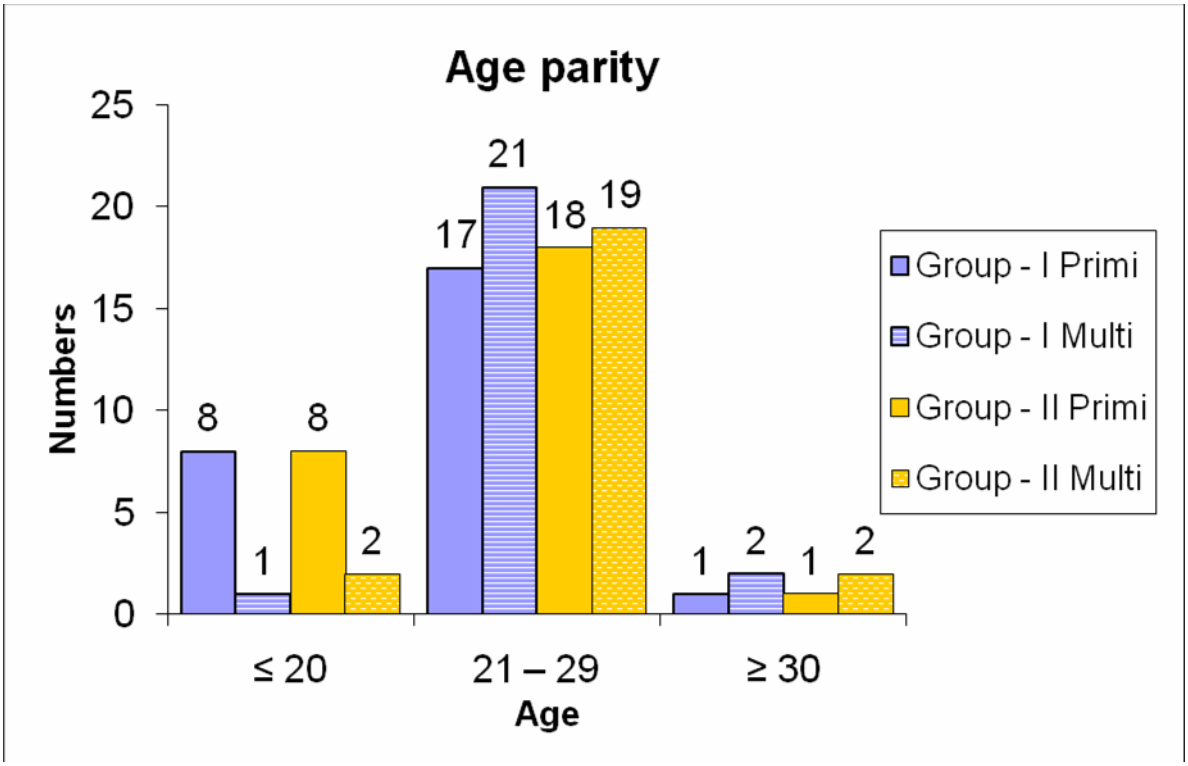
1. Patients who delivered vaginally after 48 hours of start of induction.
2. Patients who underwent caesarean section.

RESULTS AND OBSERVATION

ANALYSIS OF THE RESULTS

AGE AND PARITY DISTRIBUTION

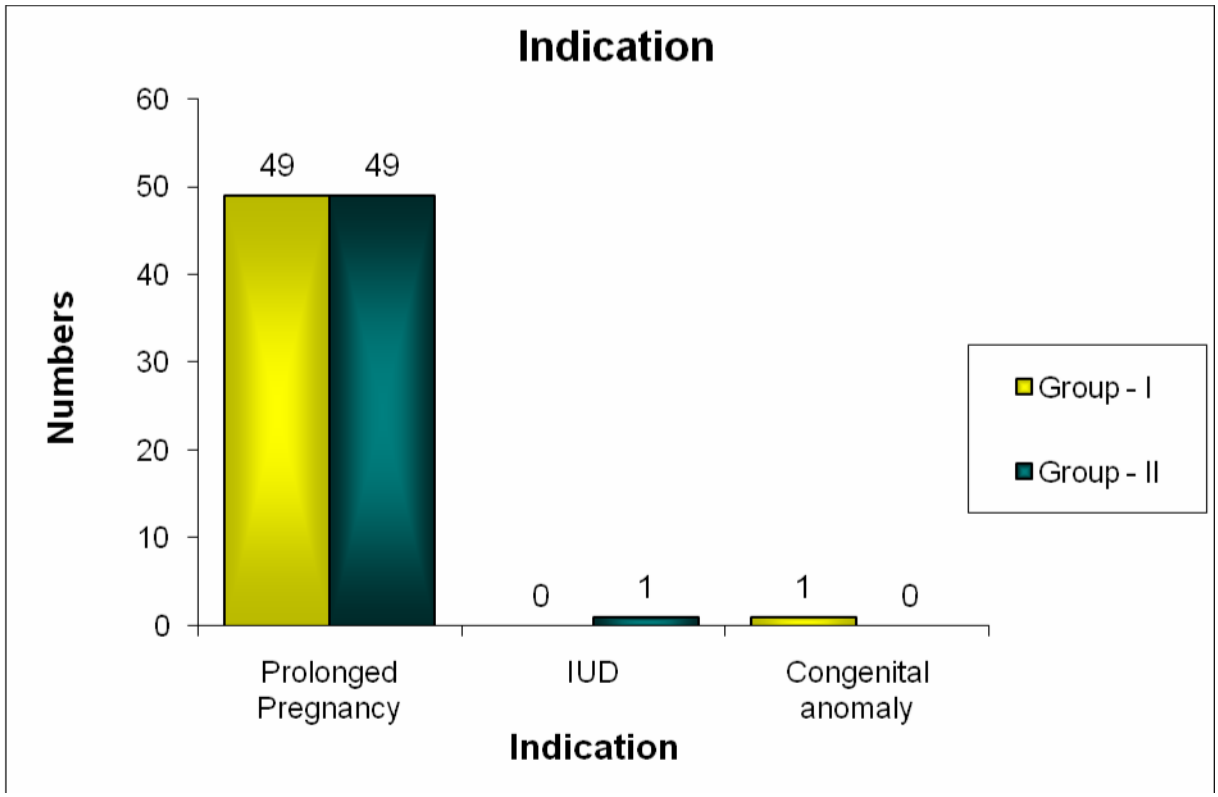
Age group (Years)	Group - I		Group - II	
	Primi	Multi	Primi	Multi
≤ 20	8 (16 %)	1 (2 %)	8 (16 %)	2 (4 %)
21 – 29	17 (34 %)	21 (42 %)	18 (36 %)	19 (38 %)
≥ 30	1 (2 %)	2 (4 %)	1 (2 %)	2 (4 %)
Total	26 (52 %)	24 (48 %)	27 (54 %)	23 (46 %)



Age and parity distribution of women included in this study were comparable in both mifepristone and PGE_2 gel group.

INDICATION FOR INDUCTION OF LABOUR

Indication	Group - I	Group - II
Prolonged Pregnancy	49 (98 %)	49 (98 %)
IUD	0	1 (2 %)
Congenital anomaly	1 (2%)	0
Total	50 (100 %)	23 (46 %)

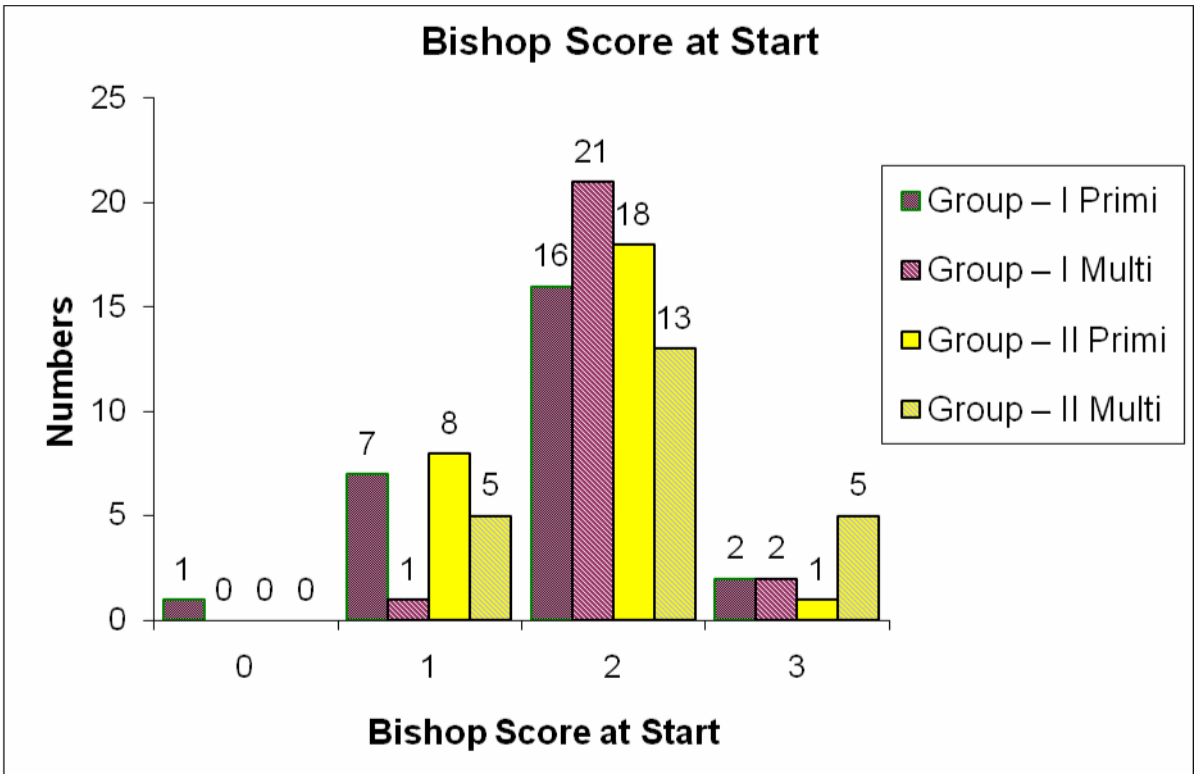


The major indication for induction was prolonged pregnancy 49 (98 %) in each group and 1 (2 %) was induced for term IUD in mifepristone group

and 1 (2 %) was induced for congenital anomaly in term baby in PGE_2 gel group

BISHOP SCORE AT THE START OF STUDY

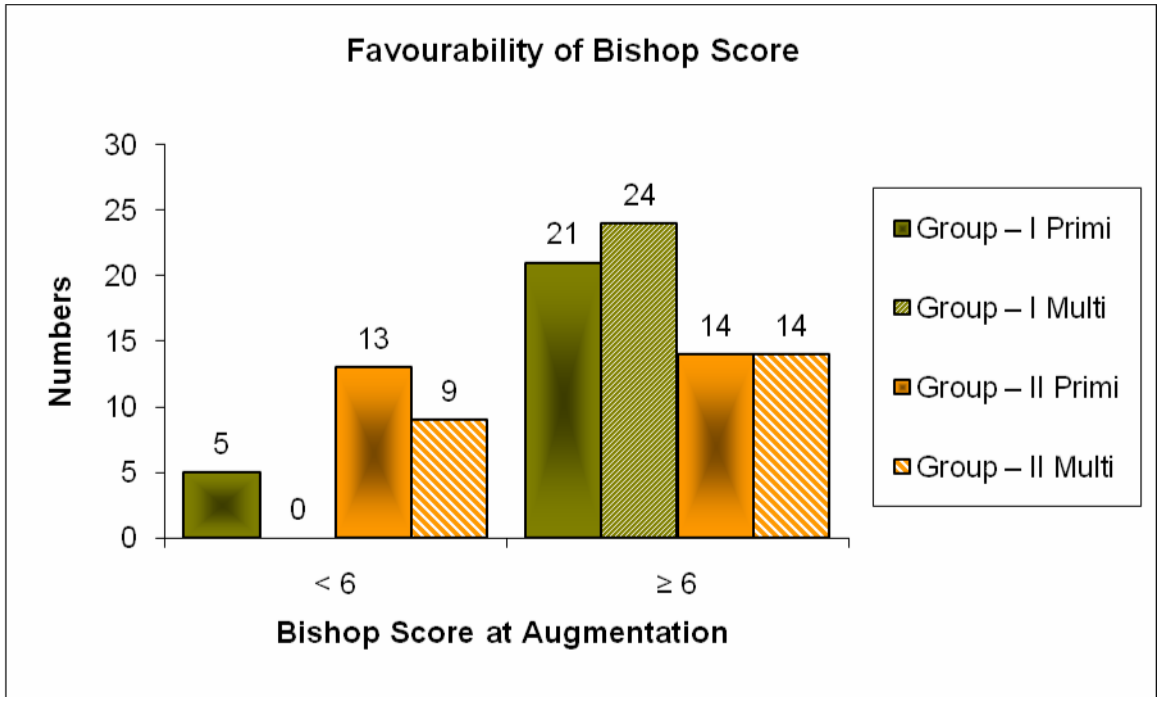
Score	Group – I		Group – II	
	Primi	Multi	Primi	Multi
0	1 (2 %)	-	-	-
1	7 (14 %)	1 (2 %)	8 (16 %)	5 (10 %)
2	16 (32 %)	21 (42 %)	18 (36 %)	13 (26 %)
3	2 (4 %)	2 (4 %)	1 (2 %)	5 (10 %)



All the mothers in both groups had initial Bishop Score of 0 to 3 before preinduction cervical ripening.

FAVOURABILITY OF BISHOP SCORE

Score at augmentation	Group – I			Group – II		
	Primi	Multi	Total	Primi	Multi	Total
< 6	5 (10 %)	0	5 (10%)	13 (26 %)	9 (18 %)	22 (44%)
≥ 6	21 (42 %)	24 (48 %)	45 (90%)	14 (28 %)	14 (28 %)	28 (56%)



FAVOURABILITY OF BISHOP SCORE

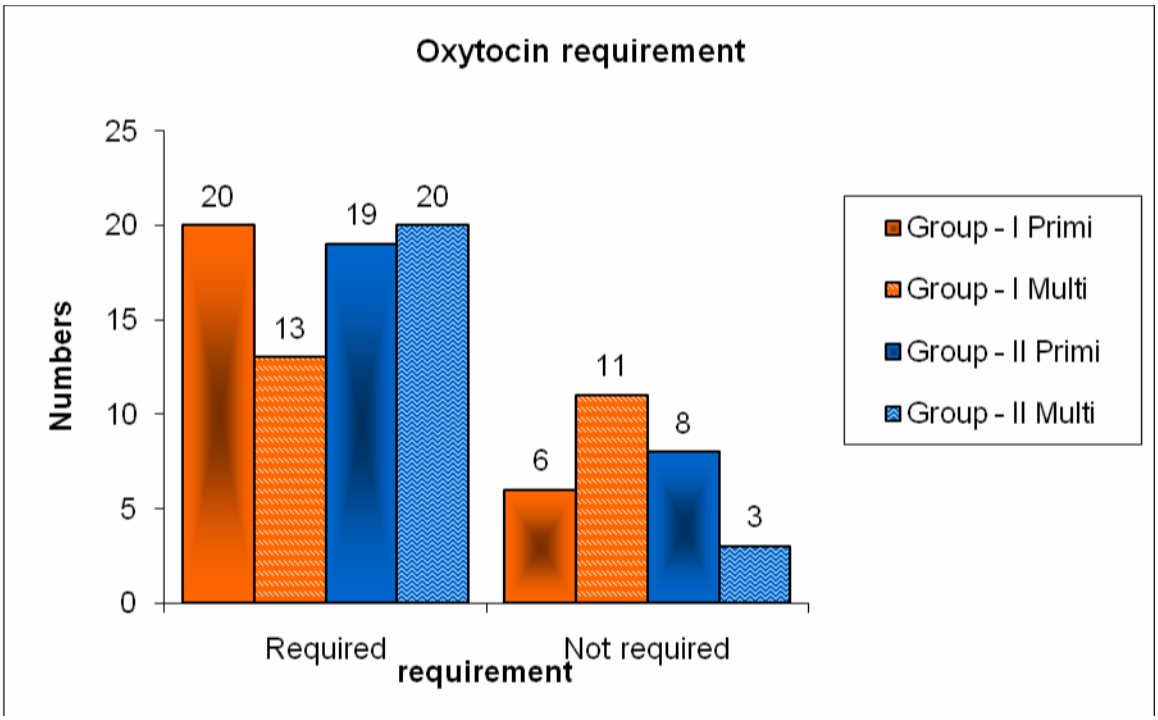
	Group	Mean	Std. Deviation	Std. Error mean
Bishop score start	Group – 1	1.8800	0.55842	0.07897
	Group – II	1.8600	0.60643	0.08576
Bishop score at Augmentation	Group – 1	6.8800	1.46580	0.20730
	Group – II	5.5000	2.29685	0.32482
Bishop score difference	Group – 1	5.0000	1.55183	0.21946
	Group – II	3.6400	2.14533	0.30340

Mean increase in Bishop score in mifepristone group is 5 whereas 3.6 in PGE_2 gel group.

- P - Value for Bishop score at start 0.864 which is not significant.
- P - Value for Bishop score at augmentation 0.001 which is significant.
- P - Value for Bishop score difference 0.000 which is significant.

AUGMENTATION WITH OXYTOCIN

Augmentation	Group - I			Group - II		
	Primi	Multi	Total	Primi	Multi	Total
Required	20 (40 %)	13 (26 %)	33 (66%)	19 (38 %)	20 (40 %)	39 (78%)
Not required	6 (12 %)	11 (22 %)	17 (34%)	8 (16 %)	3 (6 %)	11 (22%)



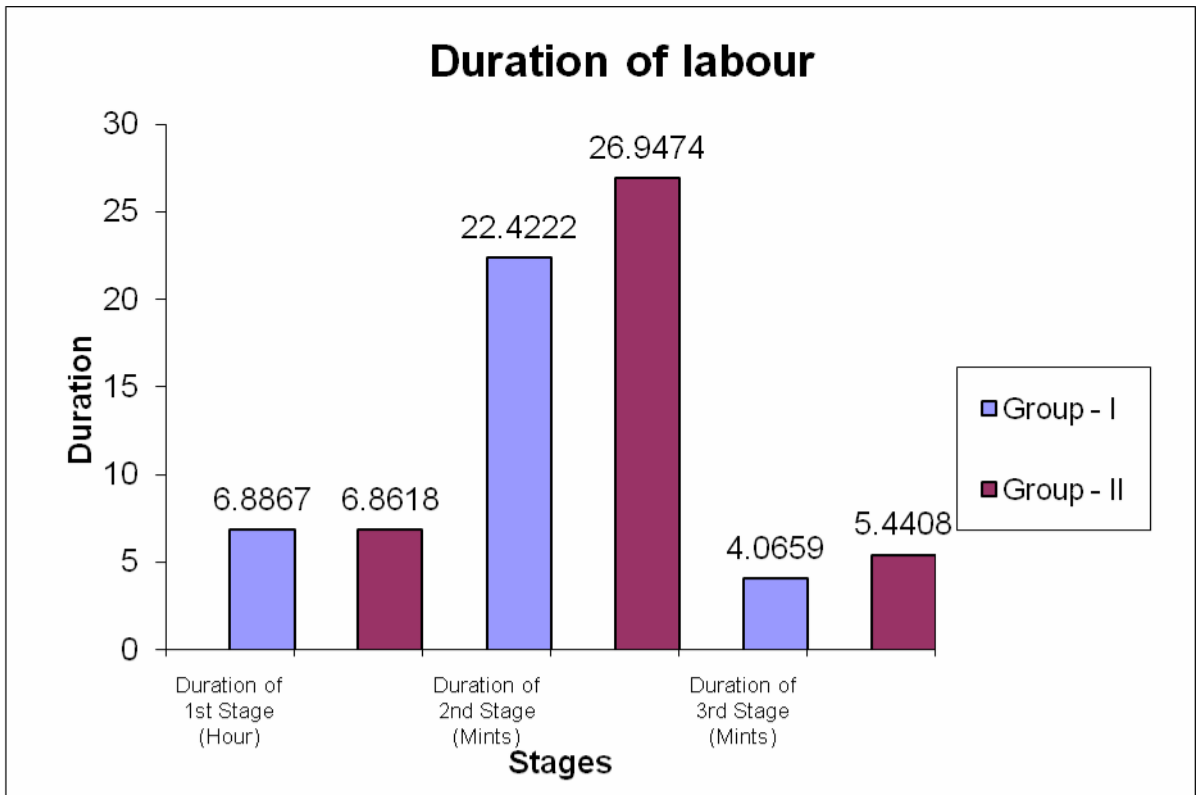
In the mifepristone group among the 6 primigravida who were not in need of oxtocin augmentation 4 (8%) had vaginal delivery within 24 hours of oral mifepristone administration. Shortest drug administration to delivery interval was 12 hours and 5 minutes. Among the 11 multigravida who were not in need of oxytocin augmentation in the mifepristone group 9 (18%) had vaginal delivery with in 24 hours of oral mifepristone, of which 4 (8%) had

delivery within 10 hours. Shortest drug administration to delivery interval was 5 hours 54 minutes.

Whereas in PGE_2 gel group 11 antenatal women which includes 8 primigravida and 3 multigravida who were not in need of oxytocin augmentation were those delivered by cesarean section. In other words in PGE_2 gel group all women who had vaginal delivery were in need of oxytocin augmentation.

MEAN DURATION OF LABOUR

	Group	Mean	Std. Deviation	Std. Error mean	P value
Duration of 1st Stage (Hour)	Group – 1	6.8867	2.12457	0.31671	0.951 (NS)
	Group – 2	6.8618	1.41495	0.22954	
Duration of 2nd Stage (Mints)	Group – 1	22.4222	5.19829	0.77492	0.001 (S)
	Group – 2	26.9474	6.40501	1.03903	
Duration of 3rd Stage (Mints)	Group – 1	4.0659	1.20309	0.18137	0.000 (S)
	Group – 2	5.4408	1.30596	0.21185	
DD intervial	Group -1	18.7341	10.04693	1.48134	0.000 (S)
	Group -2	11.4784	3.85563	0.62547	



Duration of II and III stage of labour were shorter in mifepristone group with statistical significance. Duration of I stage \shorter in PGE_2 gel group which is not statistically significant Drug administration to delivery interval shorter with PGE_2 gel group with statistical significance.

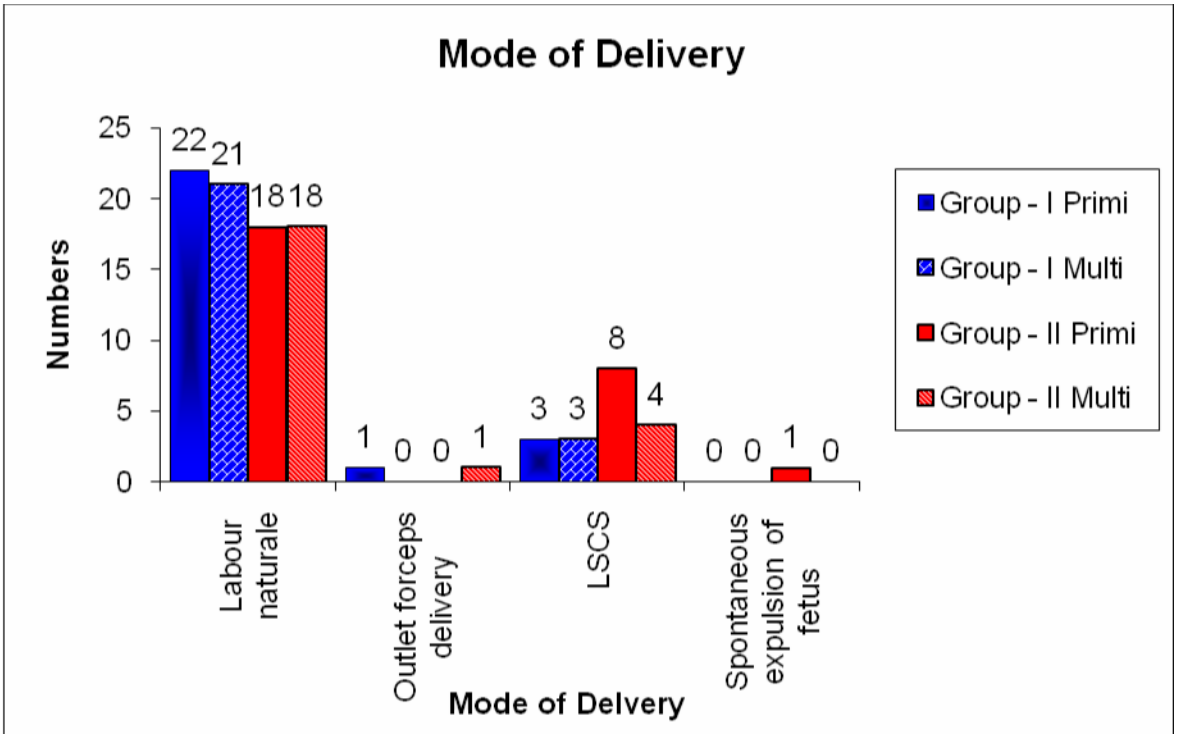
Stages of Labour	**Group - I**		**Group - II**	
	Primi	**Multi**	**Primi**	**Multi**
I – Stage (hours)	7.8542	5.7810	6.9816	6.7421
II – Stage (Minutes)	23.3750	21.3333	27.4211	26.4737
III – Stage (Minutes)	4.5435	3.5429	5.7342	5.1474
Drug administration to delivery interval (hours)	21.6292	15.2876	12.5142	10.4426

	Group –I 'P' Value	**Group –II 'P' Value**
I Stage	0.001(Significant)	0.609 (Not Significant)
11 Stage	0.192(Not Significant)	0.655 (Not Significant)
III Stage	0.005 (Significant)	0.169(Not Significant)
DD interval	0.031 (Significant)	0.098(Not Significant)

Statistically significant shorter duration of I and III stage of labour in multigravda in miferpristone group whereas no statistical difference in duration of labour among primigravida and multigravida in PGE_2 gel group.

MODE OF DELIVERY

Mode of Delivery	Group - I			Group - II		
	Primi	Multi	Total	Primi	Multi	Total
Labour naturale	22 (44 %)	21 (42 %)	43 (86%)	18 (36 %)	18 (36 %)	36 (72%)
Outlet forceps delivery	1 (2 %)	-	1 (2%)	-	1 (2 %)	1 (2 %)
LSCS	3 (6 %)	3 (6%)	6 (12%)	9 (18 %)	3 (6 %)	12 (24 %)
Spontaneous expulsion of fetus	-	-	-	1 (2 %)	-	1 (2 %)
Total	26 (52 %)	24 (48 %)	50 (100%)	27 (54 %)	23 (46 %)	50 (100 %)



Cesarean section rate was higher in PGE_2 gel group which was 24 % when compared to mifepristone group in which it was 12 %.

INDICATION FOR LSCS

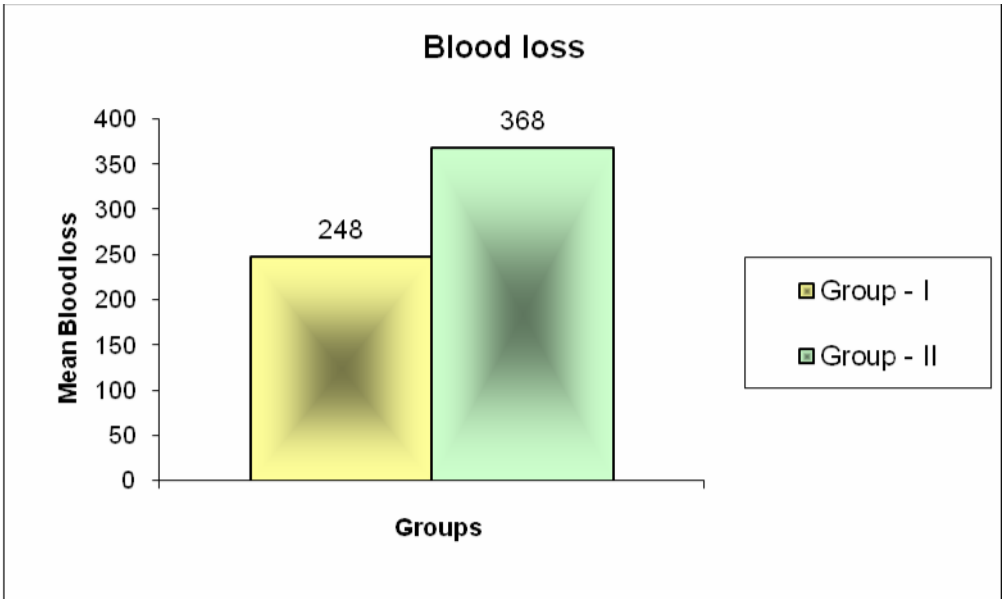
Indication for LSCS	Group - I		Group - II	
	Primi	**Multi**	**Primi**	**Multi**
Failed induction	1 (2 %)	-	3 (6 %)	1 (2%)
Fetal distress	2 (4 %)	3 (6 %)	6 (12%)	2 (4%)
Total	3 (6 %)	3 (6 %)	9 (18 %)	3 (6 %)

In the mifepristione group 3 (6%) primigravida were delivered by cesarean section of which 1 (2%) was done for failed induction and 2 (4%) were done for fetal distress whereas in multigravida 3 (6%) were delivered by cesarean section for fetal distress.

In the PGE_2 gel group among 9 (18%) primigravida delivered by cesarean 3 (6%) were done for failed induction and 6 (12%) were done for fetal distress whereas in multigravida 1(2%) were done for failed induction and 2 (4%) were done for fetal distress.

MEAN BLOOD LOSS

Blood Loss	Group - I	Group - II
Mean Blood loss (ml)	248	368
Standard Deviation	160.66190	222.63725
Standard Error mean	22.72102	31.48566

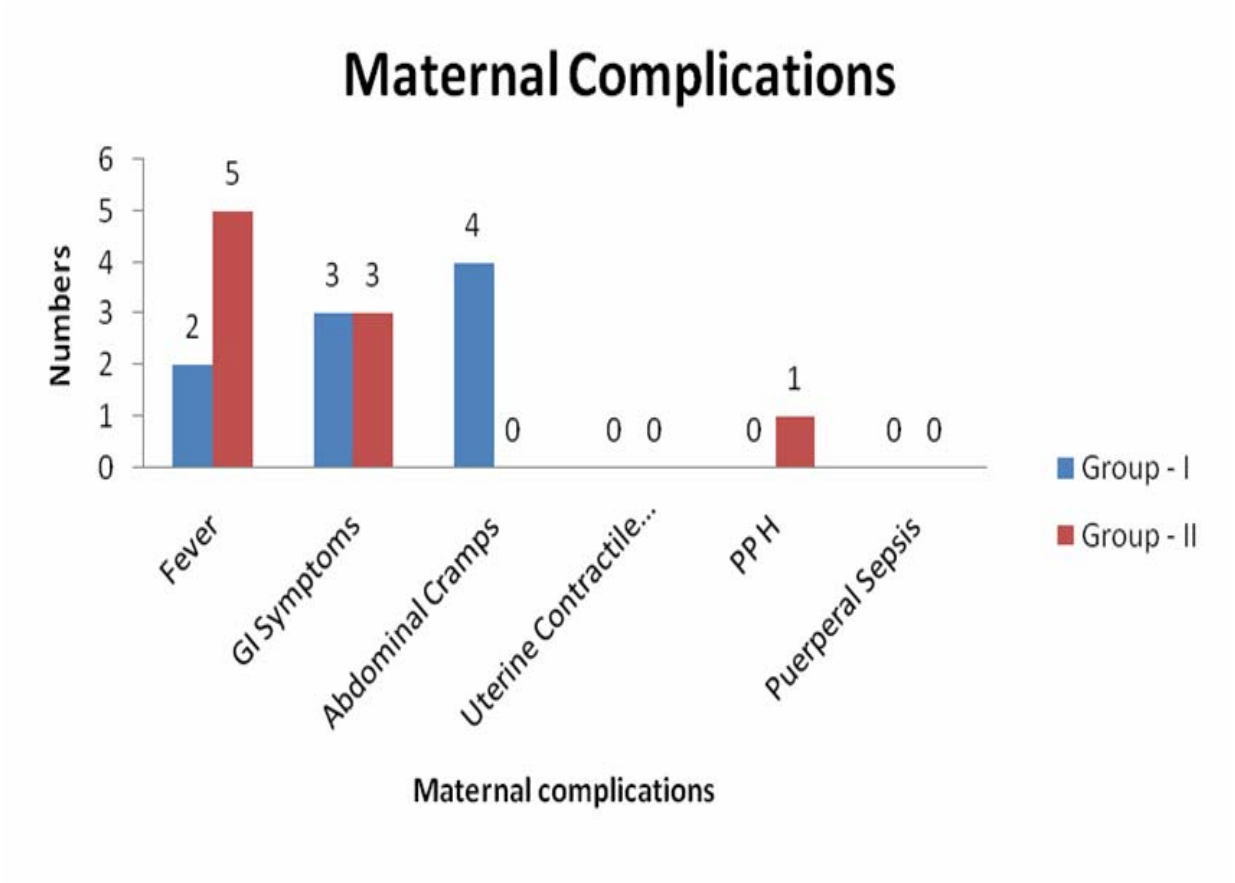


P value : 0.03 (significant)

Mean blood loss in mifepristone group was less when compared to PGE_2 gel In PGE_2 gel group 1 (2%) Primigravida had atonic PPH – blood loss of 1250ml which was controlled with uterotonics.

MATERNAL COMPLICATIONS

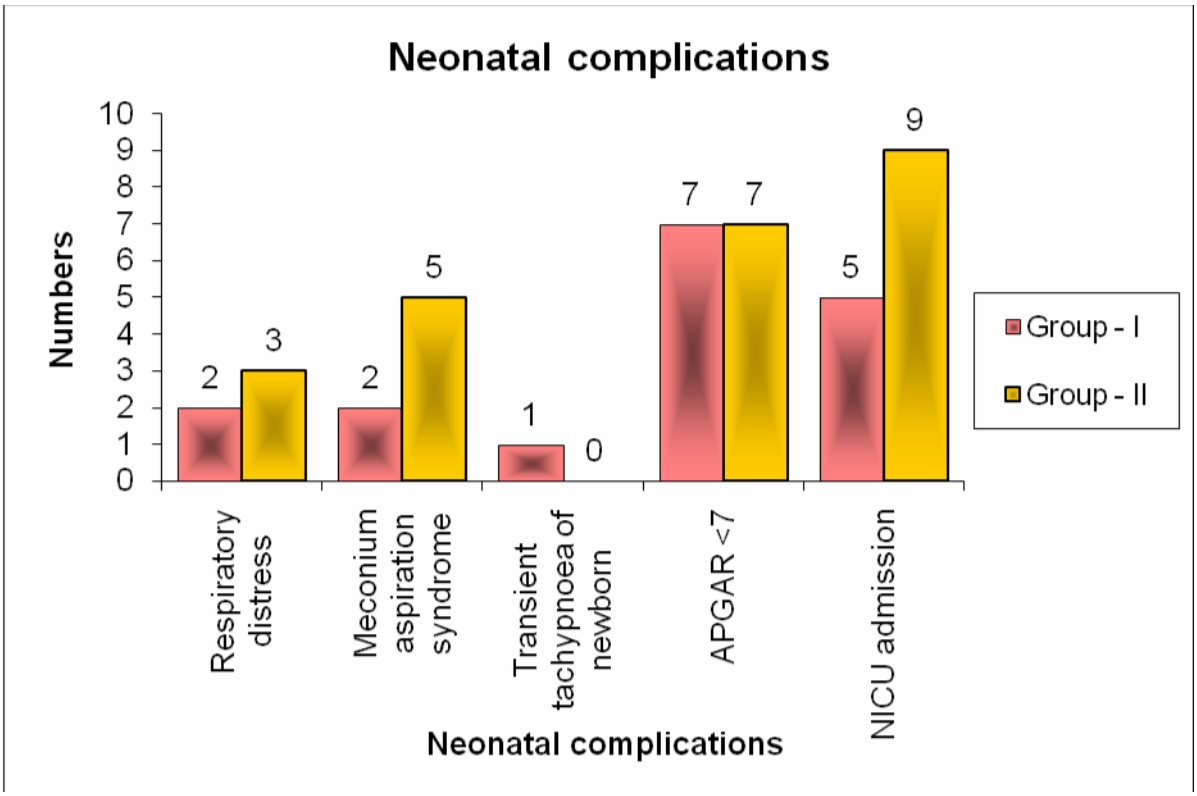
Maternal Complications	Group - I	Group - II
Fever	2 (4 %)	5 (10 %)
GI symptoms	3 (6 %)	3 (6 %)
Abdominal cramps	4 (8 %)	-
Uterine contractile abnormalities	-	-
PP H	-	1 (2 %)
Puerperal sepsis	-	-



Maternal Complications were similar in both groups.

NEONATAL COMPLICATIONS

Neonatal Complications	Group - I	Group - II
Respiratory distress	2 (4 %)	3 (6 %)
Meconium aspiration syndrome	2 (4 %)	5 (10 %)
Transient tachypnoea of newborn	1 (2 %)	-
APGAR <7	7 (14 %)	7 (14 %)
NICU admission	5 (10 %)	9 (18 %)



NICU admission was 18% in PGE_2 gel as compared to 10% in mifepristone group. In PGE_2 gel group one neonate was admitted for low birth weight.

Apgar Score at 1 minute and 5 minute were similar in both groups. 7 (14%) neonates in each group had Apgar Score < 7 at 5 minutes following birth.

DISCUSSION

DISCUSSION

Table 1

Sl. No.	Study	Year	Dosage Schedule	Control	Wait period
1.	Wing DA at al	2002 (180)	200mg of mifepristone oral dose followed by intravaginal misoprostol 25 microgr ams every 4th hourly or IV oxytocin.[17]	Placebo	24 Hrs
2.	LiL et al	1996	150 or 200mg mifepristone in the 1st 2 or 3 days & on 4th day misoprostol was added successively in 100-300 micro gram dosage.[14]	-	3 Days
3.	SuH et al	1996 (124)	50mg mifepristone 12th hourly for 2 days followed by prostaglandin or oxytocin.[15]	-	48 Hrs
4.	Frydam R et al	1992 (120)	200mg mifepristone on day 1 and 2 followed by augmentation with prostaglandin on day 4.[10]	Placebo	4 Days
5.	Giacolone PL et al	1992	400mg of mifepristone as a single single oral dose.[16]	Placebo	48 Hrs
6.	Elliot et al	1998 (83)	50-200mg mifepristone as a single oral dose.[19]	Placebo	24Hrs interval for 72 hrs
7.	Padayachi T et al	1989	400mg mifepristone as a single oral dose.[20]	-	72 Hrs
8.	This study	2010	200mg mifepristone as a single oral dose.	PGE_2	24 Hrs

In this study mifepristone given as 200mg single dose orally and observation period of 24 hours similar to the wing DA etal and Elliot et al study in which mifepristone were compared with placebo whereas PGE_2 gel in this study.

Table - 2

No	Study	Year	Need for augmentation
1.	LiL et al	1996	80%
2.	SuH et al	1996	Decreased
3.	Frydman R et al	1992	decreased
4.	Wing DA et al	2002	67%
5.	This study	2010	66%

In this study 66% required oxytocin, which was consistent with prior studies.

In this study mean duration of first stage was less than 8 hours and second stage duration was less than 30 minutes. These results were consistent with WHO standards.

In this study 36 (72%) women 32% primigravida and 40% multigravida delivered vaginally within 24 hours and totally 44 (88%) women 46% primigravida and 42% multigravida delivered vaginally within 48 hours which was consistent with Wing DA et al study.

Table - 3

Sl. No.	Study	Year	Incidence of vaginal delivery
1.	LiL et al	1996	80.88%
2.	SuH et al	1996	22.58% (vs 4.84% of control group)
3.	Giacalone PL et al	1992	80.5%
4.	Wing DA et al	2002	87.5%
5.	This study	2010	88%

In this study vaginal delivery rate was 88% (46% primigravida and 42% multigraavida) the results were consistent with above mentioned studies.

In this study intrapartum complications like hypertonus, tachysystole or hyperstimulation were not encountered, which was consistent with Wing DA et al study. Meconium passage was encountered in 4% and NICU admission was 10%.

In this study the success of induction was vaginal delivery within 48 hours. Success rate was 88% which was consistent with 87.5% success rate in wing DA et al study and 80.5% in Giacalone et al study.

In this study success of induction in relation to change to favourable Bishop score of 6 or more was seen in 90% (42% in primigravida and 48% in multigravida) which was consistent with Frydman et al study, Giacalone et al study, Wing DA et al study and Elliot et al study.

In this study failed induction in terms of cesarean section or vaginal delivery after 48 hours of ripening was seen in 12% among which 1 primigravida underwent cesarean section for failed induction. These results were consistent with Giacalone et al study, Elliot et al study and wing DA et al study in which failed induction rate was 9.2%.

Mifepristone is administered orally which is very convenient and antenatal mothers can be ambulant when compared to cumbersome PGE_2 gel administration which has to be instilled endocervically with strict asepsis by technically skilled personnel and needs observation in left lateral position.

Mifepristone is stored at room temperature whereas PGE_2 gel storage needs cold chain maintenance the cost of mifepristone is comparable to PGE_2 gel. Further need of oxytocin for augmentation is very much reduced with mifepristone when compared to PGE_2 gel.

SUMMARY

SUMMARY

The safety and efficacy of oral mifepristone as a preinduction cervical ripening agent is assessed in this study and compared with PGE_2 gel. 100 antenatal mothers admitted at Government Kilpauk Medical Hospital, who needed elective induction, satisfying the inclusion criteria were recruited into two groups and each were given oral mifepristone 200mg or endocervical PGE_2 gel 0.5mg for cervical ripening and augmented with oxytocin. This study documents the success of induction, details of parturition, maternal and neonatal outcome.

This study revealed that

- Mothers in both groups had Bishop score of 0 to 3 at the start of study. 90% (42% primigravida and 48% multigravida) had favourable Bishop score in mifepristone group whereas only 56% (28% primigravida and 28% multigrovida) in PGE_2 gel group.

- Oxytocin augmentation not needed in 26% (8% primigrovida and 18% multigravida) in mifepristone group who had vaginal delivery whereas all mothers who had vaginal delivery in PGE_2 gel group required oxytocin.

- Duration of II and III stage of labour shorter in miferpristone group .

- Cesarean section rate was 12% in mifepristone group whereas 24% in PGE_2 gel group.
- Blood loss was less in mifepristone group.
- Neonatal complications and neonatal admissions were lesser in mifepristone group.
- Drug administration to delivery interval shorter with PGE_2 group.
- Maternal complications were similar in both groups.
- The outcome of induction in this study reveals that the mifepristone was successful in 88% in achieving vaginal delivery whereas PGE_2 gel was successful in 76%.

CONCLUSION

CONCLUSION

This study reveals that oral mifepristone is very safe and an effective drug for preinduction cervical ripening. It has an added advantage of ease of administration, better patient compliance and acceptance, reduced oxytocin requirement, shorter duration of II, III stages of labour, less blood loss with an overall success rate of 88%. The drug has no untoward side effects on uterine contraction and no major maternal complications. This drug has safe nenatal outcome.

This drug is more effective in multigravida when compared to primigravida Hence mifepristone offers advantages over PGE_2 gel which is currently used for preinduction cervical ripening.

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PROFORMA

PROFORMA

Name:	Age	DOA:
		DOD:
Address:	IP.No	L.M.P:
	SES	E.D.D:

HISTORY:

- ❖ History of Presenting complaints — Booked Case: Yes/No.
- ❖ Obstetric History Gr P L A
- ❖ Menstrual History
- ❖ Past Medical / Surgical History
- ❖ Personal History
- ❖ Family History

GENERAL PHYSICAL EXAMINATION

Height	Weight	BMI	
Pallor	Edema		
Pulse	BP	RR	Temperature
CVS	RS	Breast	Thyroid

Per Abdomen – Uterine Size — Activity

- Lie — Presentation — Position
- FHR

Per Speculum

Per Vaginum - Cx Dilatation Position Consistency
Effacement
Integrity of membranes
Presentation and Station
Pelvic Assessment

INVESTIGATIONS

1. Hb%
2. Urine-albumin
   Sugar
   Deposits
3. Bloodgroup&Rh typing
4. Blood-urea
   -Sugar
5. Serum creatinine
6. HIV, VDRL, HB_SAG
7. Obstetric scan – single, live/dead, fetus
   - Cardiac activity&fetal movements
   - B.P.D- cms weeks days
   - F.L - cms weeks days
   - Placenta-fundal anterior/posterior
   - Grade maturity
   - Liquor adequate/not
   - Obvious congenital abnormalities

Bishop score on admission-

Indication for induction-

Date and time of induction-

Bishop score at time of induction-

Drug used for preinduction ripening-PGE_2 gel/

- mifepristone

Wait period after induction

Bishop score at time of augmentation

Augmentation with oxytocin- yes/no

Dosage needed

DURATION OF LABOUR

First stage (Hrs)

Second stage (Mts)

Third stage (Mts)

NATURE OF DELIVERY

Labour Natural/labour natural with episiotomy	Insrumental delivery			Lscs Indication
	Outlet forceps	Low midcavity forceps	Vacuum delivery	

Amount of blood loss at III stage

Drug administration to delivery interval

Complications-Maternal

Nausea/vomiting/diarrhea

Headache/hyperthermia/fever

Abdominal cramps

Chorioamnionitis/endometritis/puerperal sepsis,

Uterine contraction abnormalities-

Tachysystole/hypertonus/Hyperstimulation.

Any Treatment Given

Intrapartum &Fetal Complications

1. Fetal heart rate abnormalities
2. Meconium passage-thin/thick

BABY

Birth weight

Apgar 1’ 5’

Congenital anomalies if any

Neonatal resuscitation

Neonatal admissions

Fetal complications-Meconium aspiration syndrome

-Hyperbilirubinemia

-Others

MASTER CHART

PG E2 GEL

Sl. No.	Name	Age	IP.No	Booked /Unbooked	SES	Primi/Multi	Indication for induction	Bishop's score		Augmentation with oxytocin	Amount of Oxytocin (Units)	Duration		D.D Interval (Hr)	Mode of Delivery	III Stage Duration (Mts)	Blood Loss (ML)	Complication		B.wt (Kg)	Apgar	
								At start	At Augmn.			I Stage (Hr)	II Stage (Mts)					Maternal	Fetal		1"	5"
1	Maheswari	21	2501	B	IV	P	PP	2	6	Yes	5	9	25	20.02	LN	5.5	300	Nausea	-	3.22	6	8
2	Revathi	23	2539	B	V	P	PP	2	8	Yes	5	6.3	30	8.25	LN	6	250	fever	-	2.88	7	8
3	Lily	23	2497	B	IV	M	PP	3	6	Yes	2.5	7	20	9.3	LN	3	300	-	-	4	6	8
4	Umamaheswari	19	2563	B	IV	P	PP	2	4	Yes	5	8.3	35	15.1	LN	5	300	-	-	3	7	8
5	Vanitha	24	3800	B	IV	M	PP	2	6	Yes	2.5	6	28	9.25	LN	7	350	-	-	3.3	7	8
6	Seetha	26	4260	B	IV	M	PP	2	6	Yes	2.5	6	23	8.49	LN	6	300	-	-	2.5	7	8
7	Madhavi	21	4370	B	V	P	PP	2	2	No	-	-	-	-	LSCS	-	750	-	-	2.93	5	7
8	Saraswathy	24	4376	B	IV	P	pp	1	4	Yes	10	7.3	22	15.13	LN	6	200	-	-	2.45	6	8
9	Vanishree	26	4390	B	V	P	IUD	2	4	Yes	5	5.15	30	14.45	SP. EXPLN	5	150	-	-	3.19	-	-
10	Jenifer	24	4510	B	V	M	PP	1	8	Yes	2.5	7.3	20	8	LN	5	300	fever	-	2.3	7	8
11	Buvaneswari	25	4577	B	IV	P	PP	2	6	Yes	5	8.3	40	11.43	LN	5	200	-	-	2.25	7	8
12	Bagyalaksmi	19	4051	B	IV	P	PP	2	8	Yes	5	6	25	8	LN	5.4	250	-	-	2.75	6	8
13	Reka	18	6294	B	V	P	PP	2	4	Yes	5	7.3	23	15.07	LN	8	200	-	-	2.18	5	7

NICU Admission
No
No
No
No
No
No
No
No
No
No
No
No
No

14	Murugmmal	21	4231	B	V	P	PP	1	3	No	-	-	-	-	LSCS	-	700	-	FHA MSL	3.01	4	6	Yes
15	Faritha	27	4469	B	IV	M	PP	2	6	Yes	2.5	8.3	30	12.15	LN	5.15	300	-	-	3.2	6	8	No
16	swathi	21	6640	B	IV	P	PP	1	8	Yes	5	5.3	22	7.19	LN	5	250	-	-	3.5	4	6	Yes
17	Revathy	21	7622	B	IV	M	PP	2	4	Yes	2.5	6	22	14.16	LN	3.5	300	-	-	3.09	6	7	No
18	Sathya	28	7726	B	IV	M	PP	2	8	Yes	2.5	5	30	8.45	LN	5	300	-	-	3.05	7	8	No
19	Uvarani	24	7743	B	V	P	PP	1	9	Yes	5	5.3	25	7.33	LN	5	250	-	-	1.3	4	5	Yes
20	Jeyakodi	21	7855	B	V	P	PP	2	6	Yes	5	6.5	35	10.35	LN	7	300	-	-	2.43	6	7	No
21	Alamelu	25	7885	B	IV	P	PP	2	8	Yes	5	6	20	8.32	LN	5	150	-	-	3.61	6	8	No
22	Shameem	19	7801	B	V	P	PP	2	8	Yes	5	6	20	9.09	LN	5.3	250	-	-	2.98	6	8	No
23	Tamilselvi	19	7757	B	IV	P	PP	2	8	Yes	5	6.3	22	9.46	LN	5.15	250	-	-	2.25	6	8	No
24	Prema	23	7857	B	IV	M	PP	2	9	Yes	2.5	6	25	8.2	LN	5.5	250	-	-	2.75	8	9	No
25	Indumathi	30	7770	B	IV	M	PP	2	9	Yes	2.5	5	28	8.01	LN	8	250	-	-	2.65	6	8	No
26	Lakshmi	22	7963	B	V	M	PP	2	8	Yes	2.5	6	23	9.56	LN	5	150	-	FHA	2.4	5	6	Yes
27	Vijayalakshmi	35	5724	B	V	P	PP	2	2	No	-	-	-	-	LSCS	-	750	fever	-	3.35	7	8	No
28	Buveneswari	20	7395	B	IV	P	PP	1	3	No	-	-	-	-	LSCS	-	1250	PPH	FHA MSL	3	4	6	Yes
29	Muthulakshmi	25	7817	B	V	P	PP	2	4	No	-	-	-	-	LSCS	-	750	-	FHA MSL	2	6	8	Yes
30	Reka	23	7840	B	IV	M	PP	2	2	No	-	-	-	-	LSCS	-	600	-	FHA	3.25	7	8	No
31	Banu	30	7826	B	IV	P	PP	1	3	No	-	-	-	-	LSCS	-	600	-	FHA MSL	2.5	5	7	No
32	Savithri	27	7710	B	IV	P	PP	2	2	No	-	-	-	-	LSCS	-	750	-	FHA MSL	2.5	6	8	No
33	Eswari	25	7983	B	IV	M	PP	1	2	No	-	-	-	-	LSCS	-	600	-	-	3.02	6	8	No

34	Radhika	32	8019	B	IV	M	PP	1	1	No	-	-	-	-	LSCS	-	700	-	-	3.3	6	8	No
35	Sumathi	33	8183	B	V	M	PP	2	4	Yes	2.5	8.3	35	14.15	LN	7.1	250	-	-	2.3	5	7	No
36	Bagyalaksmi	20	8184	B	IV	P	PP	1	6	Yes	2.5	10	42	18.15	LN	8	300	-	-	2.69	7	8	No
37	Nadhiya	19	8195	B	IV	P	PP	2	6	Yes	5	8.3	38	13.28	LN	7.15	250	fever	-	2.87	7	8	No
38	Sumathi	22	8156	B	IV	M	PP	1	4	Yes	2.5	7.3	26	10.1	LN	6.5	300	-	-	2.355	6	8	No
39	Bavani	25	8162	B	V	P	PP	2	4	Yes	2.5	9	20	24.51	LN	5.15	250	Vomiting	-	2.9	6	8	No
40	Prema	19	8190	B	V	M	PP	3	8	Yes	2.5	6	22	14.35	LN	4.3	300	-	-	2.74	6	8	No
41	Gracy	22	8168	B	V	M	PP	3	8	Yes	2.5	4.3	28	8.49	OUTLET.F.D	4	500	-	MSL	3.6	4	6	Yes
42	Sasikala	25	8169	B	IV	P	PP	1	4	No	-	-	-	-	LSCS	-	600	-	FHA MSL	2.9	5	7	Yes
43	Shameem	26	8178	B	IV	M	PP	2	6	Yes	5	-	-	-	LSCS	-	500	-	FHA MSL	2.9	4	6	Yes
44	Chilia	22	8144	B	V	M	PP	2	4	Yes	2.5	8.3	35	14.15	LN	6.3	250	fever	-	3.2	6	8	No
45	Vidhya	21	8156	B	V	M	PP	1	4	Yes	2.5	7.3	26	10.1	LN	6	200	-	-	3.16	6	8	No
46	Brinda	23	8166	B	IV	P	PP	3	8	Yes	5	6	22	14.15	LN	4.15	250	-	-	2.85	7	8	No
47	Neela	26	8175	B	IV	P	PP	2	4	Yes	2.5	6.3	25	12.49	LN	6.15	300	-	-	3	6	8	No
48	Mari	24	8185	B	V	M	PP	3	8	Yes	2.5	10	40	12.05	LN	4.3	300	-	-	3.15	5	7	No
49	Sudha	20	8196	B	IV	M	PP	3	8	Yes	2.5	8	20	9.3	LN	3	150	-	-	2.81	6	8	No
50	Kavya	26	8205	B	IV	M	PP	2	4	Yes	2.5	6	22	10.15	LN	3.15	150	Vomiting	-	2.65	6	8	No

MIFEPRISTONE

Sl. No.	Name	Age	IP.No	Booked /Unbooked	SES	Primi/Multi	Indication for induction	Bishop's score		Augmentation with oxytocin	Amount of Oxytocin (Units)	Duration		D.D Interval (Hr)	Mode of Delivery	III Stage Duration (Mts)	Blood Loss (ML)	Complication		B.wt (Kg)	Apgar		NICU Admission
								At start	At Augmn.			I Stage (Hr)	II Stage (Mts)					Maternal	Fetal		I"	5"	
1	Amudha	22	768	B	IV	P	PP	2	4	Yes	5	9	35	28.35	LN	7	250	-	-	2.92	5	6	No
2	Suganya	20	780	UB	IV	P	ANOMALOUS BABY	0	6	Yes	5	7.3	25	23.3	LN	5.3	150	-	-	1.87	-	-6	No
3	kavitha	21	841	B	IV	M	PP	2	6	No	-	-	-	-	LSCS	-	650	-	FHAMSL	3	4	6	Yes
4	Nalini	22	890	B	IV	P	PP	2	6	Yes	5	9.3	30	24.2	LN	5.3	300	Nausea	-	2.25	7	8	No
5	Mythili	20	1897	B	IV	P	PP	2	8	Yes	5	8	28	12.35	LN	5	150	-	-	2.23	6	8	No
6	Selvarani	26	3246	B	V	M	PP	2	6	Yes	5	-	-	-	LSCS	-	600	-	FHAMSL	3.4	4	6	Yes
7	Divyamohan	23	3264	B	IV	P	PP	1	8	No	-	-	-	-	LSCS	-	500	-	FHA	3.34	5	6	yes
8	Devakumari	24	4054	B	IV	M	PP	2	8	No	-	-	-	-	LSCS	-	650	-	FHA	3.34	5	7	No
9	Vishalakshi	29	4530	B	IV	M	PP	2	8	No	-	6.5	20	7.1	LN	3	150	-	-	2.65	5	7	No
10	Uma	27	4304	B	V	M	PP	1	6	Yes	2.5	9	25	22.55	LN	3.45	150	-	-	2.63	7	8	No
11	Jeyalakshmi	23	4614	B	IV	M	PP	3	6	Yes	2.5	6.3	20	20.52	LN	5	150	-	-	3	5	8	No
12	Nithya	20	4649	B	V	P	PP	3	8	Yes	5	11	20	16.1	LN	8	150	-	-	3.45	5	7	No
13	Chitra	27	4644	B	V	M	PP	2	6	No	2.5	9	23	27.3	LN	5	150	Abd. Cramps	-	3.2	7	8	No
14	Kamala	25	2560	B	IV	M	PP	3	6	Yes	-	4.15	17	19.53	LN	3	150	-	-	2.84	6	8	No
15	Kamala	28	4405	B	V	P	PP	2	4	Yes	5	7.2	20	28.53	LN	3	400	Abd. Cramps	-	2.43	6	8	No

16	Tamilselvi	21	6101	B	IV	P	PP	2	8	No	-	8.2	36	15.01	LN	5.3	150	-	-	2.9	5	7	No
17	Kavipriya	24	2225	B	V	M	PP	2	8	Yes	2.5	5.3	21	16.1	LN	5.2	250	-	-	2.8	6	8	No
18	Selvarani	21	2221	B	IV	M	PP	2	6	Yes	2.5	5.3	25	20.04	LN	3	200	-	-	3.14	6	8	No
19	Indirani	26	2249	B	IV	P	PP	2	8	Yes	5	6	25	14.15	LN	5.2	250	-	-	3	6	8	No
20	Meena	28	2462	B	IV	M	PP	2	8	Yes	2.5	4.5	22	11.15	LN	3.5	150	-	-	3	6	8	No
21	Jeyamani	20	3379	B	V	M	PP	2	6	Yes	2.5	5.3	20	26.44	LN	3.15	150	Nausea	-	3.16	6	8	No
22	Chitra	26	2930	B	IV	M	PP	2	8	No	-	5.3	30	8.53	LN	3.5	150	-	-	2.7	6	8	No
23	Rathi	23	3002	B	IV	P	PP	1	8	Yes	5	5.3	20	9.2	LN	5	250	Abd. Cramps	-	2.8	6	8	No
24	Brinda	23	3136	B	IV	M	PP	2	8	Yes	2.5	6	22	12.1	LN	3	200	-	-	3.5	6	8	No
25	Devi	21	3218	B	IV	P	PP	2	4	Yes	5	8.5	25	29.59	LN	3	150	-	-	3	6	8	No
26	Nithya	30	3220	B	V	M	PP	2	8	Yes	2.5	5.15	18	16.25	LN	4.15	150	-	-	3.2	6	8	No
27	Selvalakshmi	21	3316	B	IV	P	PP	1	6	Yes	5	10.5	25	31	LN	3.5	250	-		3.2	6	8	No
28	Nazeema	24	3260	B	IV	P	PP	2	6	Yes	5	8	22	18.25	LN	3.3	150	-	-	3	6	8	No
29	Latha	20	3261	B	V	P	PP	1	8	Yes	5	6.3	21	17.1	LN	3.5	250	-	-	3.16	6	8	No
30	Devi	22	6484	B	IV	P	PP	3	6	Yes	5	6	22	20.14	LN	3.3	100	Abd. Cramps	-	2.095	5	7	No
31	Parvathy	30	6488	B	IV	M	PP	2	6	Yes	2.5	6.3	23	21.04	LN	3	100	-	-	2.8	6	8	No
32	Chitra	23	6616	B	IV	P	PP	2	8	Yes	5	5.3	20	6.26	LN	5	150	Fever	-	2.82	6	8	No
33	Kumari	27	6636	B	IV	M	PP	2	8	No	-	3	20	6.2	LN	4	100	-	-	2.965	5	7	No
34	Chitra	20	6634	B	IV	P	PP	2	8	Yes	5	8.5	20	10.4	LN	3.5	150	-	-	2.32	7	7	No
35	Renuka	26	6579	B	IV	P	PP	1	6	Yes	5	8	23	31.5	LN	5	150	-	-	2.49	6	7	No
36	shenbagam	24	7727	B	IV	M	PP	2	8	Yes	2.5	6	20	16.52	LN	3	150	-	-	2.85	6	8	No

37	Dhanalakshmi	34	7708	B	V	M	PP	2	8	Yes	2.5	6	20	10.55	LN	3.3	200	Fever	-	2.5	7	8	No
38	Bavani	24	7797	B	IV	M	PP	2	8	No	-	4.3	20	5.54	LN	3.5	300	-	-	3	6	8	No
39	Bagyalakshmi	32	7810	B	IV	M	PP	2	8	No	-	6	20	12.05	LN	3	200	-	-	2.58	6	8	No
40	Devi	23	7822	B	V	M	PP	2	8	No	-	6	20	12.3	LN	3.15	200	-	-	3	6	8	No
41	Vedavalli	18	7836	B	IV	P	PP	2	8	Yes	5	8.3	26	14.3	LN	3	150	-	-	1.85	5	8	No
42	Rajaveni	32	7872	B	IV	P	PP	2	6	No	-	8	26	21.27	LN	6	300	-	-	2.88	6	8	No
43	Bavani	19	7899	B	IV	P	PP	1	8	No	-	6	20	16.1	LN	5	500	-	-	2.4	6	8	No
44	Sureka	21	7903	B	V	P	PP	2	8	Yes	5	6.3	20	15.45	LN	3	150	Vomiting	-	2.74	6	8	No
45	Kalyani	22	7911	B	IV	P	PP	2	8	Yes	5	8	30	15.13	Outlet	5	250	-	-	3.2	6	8	No
46	Sumalatha	23	7923	B	IV	P	PP	2	8	No	-	4.5	20	12.5	LN	3.3	250	-	-	2.85	6	8	No
47	Hemalatha	22	7930	B	V	P	PP	2	2	No	-	-	-	-	LSCS	-	600	-	TTN	3.1	5	6	Yes
48	Thenmozhi	24	7965	B	IV	M	PP	2	6	No	-	6	20	19.2	LN	3	200	-	-	2.6	6	8	No
49	Yamuna	27	8009	B	IV	M	PP	2	8	No	-	6	22	10.03	LN	3.5	200	-	-	3.05	5	7	No
50	Patchaiammal	20	8015	B	IV	P	PP	1	4	Yes	5	-	-	-	LSCS	-	750	-	FHA	2.5	5	6	Yes

Key to Master Chart

IP No. - In Patient Number
B - Booked
UB - Unbooked
TTN- Transient tachypnoea of newborn
SES - Socioeconomic status
P - Primigravida
M - Multigravida
PP - Prolonged pregnancy
FHA - Fetal heart rate abnormality
IUD - Intra uterine death
DD interval - Drug administration to delivery interval
B.wt - Birth weight
NICU - Neonatal intensive care unit
LN - Labour naturale

Key to Master Chart

Booked - 1
Unbooked - 2

Primi - 1
Multi - 2

Indication
Prolonged Pregnancy PP - 1
IUD - 2
Cong. Anomaly - 3

Augmentaion with oxytocin
Yes - 1
No - 2

Mode of delivery
LN - 1
Outlet F.D - 2
LSCS - 3
Sp. Explsn - 4

Complication
Maternal
Fevet - 1
Nausea, Vomiting - 2
Abd. Cramp - 3

Fetal
FHA - 1
FHA MSL - 2
TTN - 3

NICU admission
Yes - 1
No - 2

Key to Master Chart

IP No.	-	In Patient Number
B	-	Booked
UB	-	Unbooked
SES	-	Socioeconomic status
P	-	Primigravida
M	-	Multigravida
PP	-	Prolonged pregnancy
IUD	-	Intra uterine death
DD interval	-	Drug administration to delivery interval
B.wt	-	Birth weight
NICU	-	Neonatal intensive care unit